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SUMMARY OF RECENT ABSTRACTS*

III. MALARIA

[Continued from p. 204]

Treatment

General.—The Expert Committee on Malaria of the World Health Organization has issued reports of its first and second sessions (pp. 389, 948). The first sums up much modern work on antimalaria drugs and DDT. In the second a particularly important feature is a statement of the dosages advised for the drugs in common use (which are set out in detail in the abstract).

A series of tests of potential antimalarial drugs was carried out on 500 prisoners in the United States; most of the drugs were members of the 8-aminoquinoline group. ALVING *et al.* (p. 951) explain that the Chesson strain of *P. vivax* (with high relapse rate) was used, with *A. quadrimaculatus*. In the first paper (JONES *et al.*, p. 951) it is shown that pamaquin, pentaquine and two other drugs may act as true prophylactics, but that they did not protect all subjects; they are, however, too toxic for this purpose. Another compound, SN-10,275 is also too toxic for use (PULLMAN *et al.*, p. 952). Serious reactions occurred with pentaquine at a dose of 120 mgm. of the base each day, along with quinine (CRAIGE *et al.*, p. 953). In doses of 30 or 60 mgm. of base daily, with quinine, however, the effect on fever and on the relapse rate was very good, even in heavy infections. Pentaquine should be administered only under close medical supervision, and the daily dose should not exceed 60 mgm.; it should not be used for prolonged suppression (ALVING *et al.*, p. 953).

ALVING *et al.* (p. 954) found that the curative properties of pamaquin are shared by several analogues, but no definite conclusions can be drawn as to the specific molecular configuration required in a curative drug. Régimes which produce a high percentage of cures tend to prolong latent periods in those they fail to cure.

Under the conditions of the experiment, chloroquine proved superior to quinine and mepacrine; the dosage was 2·0 gm. in one week (PULLMAN *et al.*, p. 955). It is safe if given in recommended doses, and ALVING *et al.* (p. 956) suggest 1·5 gm. of the base [2·5 gm. of the diphosphate] in three days for the

*The information from which this series of summaries has been compiled is given in the abstracts which have appeared in the *Tropical Diseases Bulletin*, 1948, v. 45. References to the abstracts are given under the names of the authors quoted, and the pages on which the abstracts are printed.

cure of attacks of *P. vivax* or *P. falciparum* malaria, and 0·3 gm. [0·5 gm. diphosphate] each week for suppression.

Results reported by JONES *et al.* (p. 955) indicated that paludrine was not as effective as mepacrine or chloroquine in terminating acute attacks, but that it was valuable and had only negligible toxic effects. It had no synergic action with either quinine or pentaquine.

In a second series of studies on chemotherapy in human malaria, SHANNON *et al.* (p. 956) worked with the McCoy strain of *P. vivax*, which is more susceptible than the Chesson strain to quinine. They show that blood forms derived from blood inoculation, and those from sporozoite infection, are equally susceptible to quinine. The effect of quinine is correlated with its concentration in plasma, but is independent of the degree of parasitaemia. Similar results were observed (EARLE *et al.*, p. 957) when *P. falciparum* infections were induced by injection of infected blood, and therapeutic response to quinine was correlated with duration of treatment and with plasma concentration ; there was some difference in the response of another strain of *P. falciparum*. The physiological disposition and antimalarial activity of the cinchona alkaloids were studied by TAGGART *et al.* (p. 958), who showed that plasma concentrations after identical doses varied widely in different subjects, and between the different alkaloids. EARLE *et al.* (p. 959) discuss the metabolism of cinchonine.

The antimalarial action of quinacrine [mepacrine] in *P. vivax* and *P. falciparum* infections was studied by TAGGART *et al.* (p. 960), and of chloroquine and other aminoquinolines, and of pamaquin, by BERLINER *et al.* (pp. 960, 961) with results similar to those of other investigations, while ZUBROD *et al.* (p. 962) report on the physiological disposition of pamaquin, and EARLE *et al.* (p. 962) on its effect on human red blood cells. Details of these findings cannot satisfactorily be further abstracted.

EARLE *et al.* (p. 963) reached the conclusion that paludrine is extremely effective against the McCoy strain of *P. vivax*, but the Costa strain of *P. falciparum* was more resistant ; paludrine is the most active suppressive agent yet described in *P. vivax* malaria.

ANDREWS and CORNATZER (p. 396) show that cinchonine is metabolized more quickly than cinchonidine or quinine in man.

MAIER (p. 971) shows that even in patients with acute dysentery, quinine and mepacrine are absorbed normally.

MAIER *et al.* (p. 860) found little difference in the results of treatment of *P. falciparum* malaria with mepacrine (3·6 gm. in 6 days) and with quinine (210 grains in 6 days). Nervous symptoms were observed in a few patients on mepacrine.

JAILER *et al.* (p. 575) refer to the fact that excretion of quinine is increased if the urine is acid, and show that the same is true of mepacrine, chloroquine and santoquine. Administration of ammonium chloride, to render the urine acid, may therefore be useful if there are symptoms of drug toxicity.

INNES (p. 33) reports on the experience of the Army malaria research team in relation to treatment of *P. vivax* malaria with quinine, mepacrine, pamaquin and paludrine. He discusses their rapidity of action, the stages of the parasites on which they act, and their effects on relapses. For details the original should be consulted.

MONK (p. 1058) has summed up recent developments in the treatment of *P. vivax* infections. Paludrine and chloroquine are about equally effective in suppression. For the acute attacks quinine (or paludrine) and pamaquin given concurrently are very satisfactory, but quinine and pentaquine (which is rather less toxic than pamaquin) together are probably better in reducing the relapse rate.

WINCKEL (pp. 144, 145) discusses the continuing value of quinine in malaria, and suggests that the hydrochloride should be used in place of the too acid bihydrochloride for intramuscular injection, thus reducing the amount of necrosis and the chance of infection.

WINCKEL (p. 303) demonstrates that there is no good reason to think that the use of quinine in pregnancy leads to congenital defects of the ear or eye of the foetus.

MAMOU (p. 237) reports a case of intolerance to quinine; two intramuscular injections of 1 gm. gave rise to haemorrhagic purpura.

There is, in various animal tissues, especially the liver, an enzyme which acts on quinine, converting it to the 2-hydroxy derivative. CHEN (p. 397) shows that both mepacrine and pamaquin inhibit the conversion of quinine, probably by acting on the enzyme.

COATNEY *et al.* (p. 680) show that quinine sulphate in doses of 0·5 gm. daily for 4 days before infection with *P. vivax* and for 21 days thereafter suppressed the early primary attack, but that the attack occurred after an incubation period of 260–332 days. Doses of 0·25 gm. for the same period usually failed, and larger doses not continued beyond 6 days after infection also failed.

STRAHAN (p. 574) describes the treatment, based on quinine, given to the malnourished prisoners of war near Singapore during the Japanese occupation. For very heavy infections quinine was given by intravenous drip regardless of the clinical condition, at the rate of 2 gm. (in 3–4 litres) in 24 hours, and continued, if necessary, for several days. The rate of flow was 30–40 drops per minute.

FIELD *et al.* (p. 577) gave neoarsphenamine, in addition to quinine, to patients with *P. vivax* malaria in internment camps near Singapore, but did not observe any benefit from the neoarsphenamine.

CHEN and GEILING (p. 490) show that quinine and plasmoquine show a synergistic action as regards toxicity and therapeutic action, and the same is true of quinine and pentaquine. Quinine and atebrin, and atebrin and plasmoquine, act independently.

SPICKNALL and TERRY (p. 753) report good results from combined quinine-plasmoquine or quinine-pentaquine treatment in relapsing *P. vivax* malaria.

Mepacrine, etc.—MACHELLA *et al.* (p. 304) have shown that intravenous mepacrine in dilute solution (1 in 1,000 in saline) is well tolerated up to a dose of 1·0 gm., but should be given by the drip method over a period of 3–4 hours.

PARMER (p. 1058) shows that there is a considerable amount of mepacrine in the bone marrow of rabbits on the 4th day after administration, although the blood is almost free. There is, however, no apparently direct relationship between mepacrine and aplastic anaemia, which is probably a matter of idiosyncrasy.

JAILER *et al.* (p. 681) have investigated the effect of acidosis and anoxia on concentrations of mepacrine and chloroquine in blood. CO_2 acidosis increases the proportion found in plasma and red cells as against the proportion in the tissues, but anoxia has no such action.

SINGH (p. 1059) reports 83 cases of atypical lichen planus in patients who had taken mepacrine, and describes the condition; in most cases the onset was acute. He did not see this disease in persons who were not taking suppressive mepacrine, and the severity seemed to be related to the amount stored in the skin.

PERK (p. 398) discusses mepacrine psychoses, describing 23 cases seen in the Middle East. Other factors than mepacrine may have been important—emotional stress, battle stress or alcoholism. Most of the cases arose after therapeutic doses had been given (3·4 gm. in 6 days). The most frequent

symptoms were schizophrenic and manic in type, with insomnia and a change in behaviour in the early stages.

Two cases of fugue after administration of mepacrine are recorded by MACDONALD (p. 237).

HOOBLER (p. 238) reports that a number of toxic nervous symptoms occurred in a group of volunteers (not in a malaria region) who took either the usual suppressive doses of mepacrine for two weeks or rather high therapeutic doses for a few days. This is not a usual finding.

Four cases of mepacrine psychosis are described by PARANJOTHY (p. 860).

EL-DIN NOUR EL-DIN (p. 1060) reports a few cases of mepacrine psychosis.

Instead of giving the acridine drug Italchina in daily doses of 0·3 gm. for 5–7 days, BUONOMINI and MOTTA-DIANA (p. 399) used 0·5–0·6 gm. each day for 4 days for both *P. vivax* and *P. falciparum* infections, with advantage.

Paludrine.—A general review of paludrine was published in 1947 by FIELD (p. 861).

CHEN and ANDERSON (p. 491) describe the general pharmacology of paludrine.

MULLICK and GUPTA (p. 755) have given paludrine intravenously, without serious toxic symptoms.

Paludrine acts on the dividing nucleus of early schizonts of *P. vivax*. Gametocytes of *P. vivax* or *P. falciparum*, if enough of the drug is present in the blood taken up by the mosquito, fail to develop beyond the stage of encystment, and MACKERRAS and ERCOLE (p. 305) have shown that for 10 days after treatment is stopped there may be enough paludrine to affect development, but not after the 12th day.

MARSHALL (p. 49) suggests that paludrine probably acts by inhibiting the oxidation processes of the malaria parasite, and quotes the evidence on which he bases his opinion.

SHUTE and MARYON (p. 578) have examined the action of paludrine on the gametocytes of *P. falciparum*, and show that mosquitoes fed upon a patient up to 7 days after cessation of paludrine failed to become infected. This confirms earlier work by FAIRLEY and his team.

In India, 6 trials of paludrine were conducted by independent workers whose reports are reviewed together (p. 862). A comment on the whole series is offered by AFRIDI (p. 862), who shows that the disease was microscopically diagnosed in all cases, 1,283 *P. falciparum*, 481 *P. vivax*, 68 *P. malariae* and 59 mixed. Acute *P. falciparum* infections responded better than *P. vivax*, and the response of *P. malariae* was often delayed. Paludrine is as effective against Indian as against other strains, and a single dose of 0·3 gm. usually suffices for clinical cure. This dose could be used in the hospitals and dispensaries of India, and relapses could be treated as they arise, or 0·1 gm. could be taken once or twice each week.

In a trial of paludrine in cases of subtertian and benign tertian malaria in India, AFRIDI *et al.* (p. 239) found that a single dose of 300 mgm. was enough for a clinical cure of an attack, and that there was no advantage in repeating the dose for several days, or in giving mepacrine.

DE and DUTTA (p. 34) have treated a small number of patients with paludrine, and report favourably on it. Similar studies are reported by CHAUDHURI and RAI CHAUDHURI (p. 35) and by PAREKH and BOGHANI (p. 36). In these three papers both *P. vivax* and *P. falciparum* cases are recorded, and various régimes were used.

In India GHOSH and GHOSH (p. 147) also report favourably on paludrine.

VISWANATHAN and BAILY (p. 754) think that paludrine may safely be left in the hands of lay village officers for distribution in India; they obtained good results in treatment and suppression with relatively low doses.

Treatment of *P. falciparum* malaria in Sardinia with paludrine 0·3 gm. daily for 10 days, with weekly administration thereafter, was very successful in most cases, though there were some attacks after the first 5 days of treatment. BETTINI (p. 861) also reports good results in a few *P. vivax* and *P. malariae* cases.

WALLS (p. 972) thinks that in Sierra Leone paludrine should be taken in a dose of 0·1 gm. each day, for effective suppression. He prefers it to other drugs, in suppression or treatment, but in doses greater than have usually been advocated.

Paludrine promptly suppressed symptoms in 89 per cent. of patients (mostly with *P. vivax*) when 0·2 gm. was given in a single dose, and in 97 per cent. with 0·4 gm. (PINTO, p. 400).

WOODRUFF (p. 240) found that a single dose of 100 mgm. paludrine was enough to control attacks of *P. vivax* malaria (mostly relapses) in prisoners of war returned from the Far East, and that 100 mgm. taken once each week for 6 months prevented relapse in 18 of the 20 patients for 6 months after the last dose.

ANDREWS *et al.* (p. 491) found that the relapse rate was about the same after short therapeutic courses of mepacrine and paludrine, but that when a small dose of paludrine was given each week for 6 months after a therapeutic course, the relapse rate was reduced.

SCHNEIDER and MÉCHALI (p. 865) in North Africa found only slight differences in effect between paludrine, nivaquine and nivaquine B, but metachloridine gave inconstant results.

Chloroquine, etc.—The dose of chloroquine advocated in the *Bull. U.S. Army Med. Dept.* (p. 37) is 5 doses (each 0·5 gm.) in 4 days (total 2·5 gm.), and for suppression 0·5 gm. once each week. Attacks are usually promptly brought under control with this dosage, and in most *P. vivax* cases the patients become afebrile and free from parasites within 24–48 hours. There are some mild reactions—pruritus, anorexia, vertigo, etc.

WARTHIN *et al.* (p. 753) have found that in treatment and suppression of *P. vivax* infections chloroquine is as effective as mepacrine; but it is no more effective than mepacrine in preventing relapses.

YOUNG and EYLES (p. 680) show that chloroquine clears the blood of *P. malariae* (in the doses used) more quickly than mepacrine, quinine or totaquine; it also acts more quickly on *P. vivax* than on *P. malariae*.

Chloroquine was very effective in cutting short blood-induced *P. vivax* malaria when given in doses to a total of 2·5–3 gm. in 48 hours (KIERLAND and MCCREIGHT, p. 400).

Aralen is another name for chloroquine; KAMAL and ABDEL MESSIH (p. 38) gave it in dosages of 2·5 gm. in 3 days or 0·5 gm. every 4 hours to a total of 2 gm. It was effective in both *P. vivax* and *P. falciparum* infections.

LUCENA (p. 1061) reports favourably on Aralen (which is chloroquine diphosphate) in *P. vivax* and *P. falciparum* infections in Brazil.

In high doses chloroquine will produce toxic effects in rats, but FITZHUGH *et al.* (p. 973) show that these doses are higher than would be used in man; the general inference was that it is slightly less toxic than mepacrine for rats.

CRAIGE *et al.* (p. 868) report two cases in which, during a long course of chloroquine administration, a cutaneous eruption was seen which resembled that occasionally caused by mepacrine.

HALAWANI *et al.* (p. 681) write that Nivaquine C is a potent antimalarial drug which does not produce toxic symptoms in the doses they propose (1·8 gm. in 5 days). It is mainly active against schizonts; their tests were made with *P. vivax*.

Nivaquine M is useful in malaria in Tunisia, but Nivaquine C is much more so, daily doses of 0·08 gm. of base will arrest an attack and the effect on the relapse rate seems to be good (DECOURT and SCHNEIDER, p. 148).

Nivaquine, in doses of 0·3 gm. once each week is as useful in suppression as mepacrine in the same dose ; Nivaquine C, 0·1 gm. daily, gives remarkably good results, without sign of intolerance (SCHNEIDER *et al.*, p. 868).

COOPER and COATNEY (p. 147) have used the compound known as NIH-204 in *P. vivax* and *P. falciparum* malaria ; it is not as effective as quinine or mepacrine. COATNEY *et al.* (p. 150) do not recommend its use as a suppressive.

" Cam-Aqi " is a synthetic antimalarial drug which SIMEONS and CHHATRE (p. 39) have found very effective in both *P. vivax* and *P. falciparum* malaria in a single dose of 7·5–10 mgm. per kgm. of body weight ; the patients were Indians.

PULLMAN *et al.* (p. 865) report that metachloridine terminates clinical attacks of *P. vivax* malaria about as quickly as quinine, though parasites persist twice as long in the blood. It has no prophylactic effect apart from suppression.

In British Guiana KENNEY and BRACKETT (p. 240) found that metachloridine is an effective suppresant for *P. malariae* and *P. vivax* (in the doses given) but not so good for *P. falciparum*.

Pamaquin, etc.—ROSENFELD *et al.* (p. 964) have demonstrated that methaemalbumin was present in the serum of all patients who received combined pamaquin and quinine therapy, but not in those who received each drug alone, or pamaquin and mepacrine together. In further work BLAKE (p. 965) shows that haemolysis alone does not give rise to the formation of methaemalbumin, but drugs in combination do so by increasing the amount of haemoglobin broken down and by interfering with its metabolism. He regards methaemalbumin as a normal product of haemoglobin metabolism.

MONK (p. 576) shows that in *P. vivax* infections the relapse rate after quinine and pamaquin treatment was about the same as the rate after paludrine and pamaquin treatment (about 20 per cent. in 6 months), but much lower than the rates after either paludrine or pamaquin alone.

CRAIGE *et al.* (p. 33) have made a preliminary assessment of the toxicity of plasmoquine in man, and its effect on the relapse rate of *P. vivax* malaria ; details should be sought in the original.

SCHNEIDER *et al.* (p. 868) report favourably on administration of premaline in Tunisia ; 3 tablets were given once each week during May, and thereafter once every 10 days until the end of November.

Pentaquine is closely allied to pamaquin ; it was given by MONK (p. 577) to soldiers who had *P. vivax* malaria, with or without quinine. Clinical cure was rapid but half the patients showed toxic symptoms. The relapse rate was about 12 per cent. in 6 months.

STRAUS and GENNIS (p. 974) show that pentaquine is very effective in preventing relapse in *P. vivax* malaria if given in doses of 30 mgm. of base daily for 14 days, with quinine. This dosage is only half the dosage recommended previously.

Other drugs.—JANG *et al.* (p. 578) discuss the pharmacology of *Dichroa febrifuga*, a Chinese antimalarial herb.

CHOU *et al.* (p. 755) discuss the antimalarial constituents of *Dichroa febrifuga*.

By using sympatol in place of adrenaline, CASTANA and MILANI-COMPARETTI (p. 755) have successfully treated 72 cases of malarial splenomegaly according to the Ascoli method.

Anoxia in malaria develops as a result of destruction of red cells and acidosis, and RIGDON (p. 978) has found in animals that exposure to an atmosphere rich in oxygen has a useful therapeutic effect, supporting life until antimalarial

drugs have opportunity to act. The same is true of blood transfusion. Nicotinic acid dilutes the cerebral capillaries and may also be useful, but these are only adjuvants to the specific drugs.

NEWPORT (p. 237) has found that early administration of intravenous glucose saline is of great service in algid malaria; blood chlorides are often reduced in this condition.

Suppressive Treatment

ADHIKARI (p. 754) succeeded in administering suppressive mepacrine to the 48,000 staff of the Bengal Assam Railway during the transmission season of 1945, with very satisfactory results.

TRAGER (p. 398) found *P. vivax* in thick blood films of 12–25 per cent. of Negro and white soldiers in New Guinea in spite of the fact that they were taking 0·1 gm. mepacrine each day. The men had no clinical symptoms, and the incidence was rather higher in white than in Negro troops.

In a small test in the Belgian Congo VAN RIEL (p. 866) found good suppressive effect by three doses of paludrine, each of 0·1 gm., each week; but when administration was stopped shortly after the men were removed from possibility of infection, most of them developed malaria.

For children in Zanzibar, presumably African, ROBERTSON (p. 972) found that 0·1 gm. paludrine given twice each week was rather too small a dose to be completely effective in suppression.

MAIER (p. 867) thinks that one tablet of chloroquine (0·3 gm. free base) each week is effective in suppression in the Philippines.

PACKER (p. 149) has compared the suppressive action of chloroquine, paludrine and SN 8137, in *P. vivax* and *P. falciparum* infections (with two well known strains); details should be sought in the original, but all are effective, and paludrine is apparently a true causal prophylactic for *P. falciparum*.

COATNEY *et al.* (p. 150) found that sulphadiazine and sulphapyrazine have no advantage over mepacrine as suppressants of *P. vivax* and *P. falciparum*.

Repellents

CHRISTOPHERS (p. 40) sums up all previous work on mosquito repellents, and reports his own investigations under laboratory conditions, with *Aëdes aegypti* as the test mosquito. Pure dimethyl phthalate is probably the best repellent for mosquitoes and midges, but a little incorporated citronella probably helps.

In a test of a large number of repellents, MCCULLOCH and WATERHOUSE (p. 869) found dimethyl phthalate to be the best against *A. punctulatus farauti* and other mosquitoes. On the other hand, TRAVIS (p. 241) found that a mixture of repellents (dimethyl phthalate, R.612 and Indalone) gives better protection than any single one against *A. punctulatus farauti*.

Control

General.—MILLER *et al.* (p. 485) discuss the practical application of the International Sanitary Convention for Aerial Navigation with regard to transportation of anophelines into the United States. Reports show that living specimens of several vector species have been introduced, and the authors think that not more than 10 per cent. of the mosquitoes are detected in the aeroplanes.

FARRELL (p. 579) shows that during the war, in spite of precautions taken on arrival of aircraft in Brazil from West Africa, *A. gambiae* was still being introduced. One principal reason was that breeding was taking place too near the airfields in West Africa, and steps were therefore taken by British, American and French authorities, to ensure more complete control over a wider area round the airfields. Results, as judged by incidence of malaria in

the local troops, were good except in Liberia, and they had the desired effect in preventing transport of *A. gambiae*. In comment, TREDRE remarks that application of insecticide to aircraft as the sole means of prevention is unreliable. He also points out some inaccuracies in the original paper.

The whole subject of malaria control in West Africa by coastal swamp drainage has been dealt with in a monograph written by GILROY (p. 1043). This should be studied in the original. It is an account of war-time work, and is indispensable to anyone undertaking a similar task.

WALTON (p. 401), in a most important paper, has made a close examination of the effects of the extensive and careful larvicide campaign carried on in Freetown, Sierra Leone, during the war. The number of female *A. gambiae* caught in houses was greatly reduced, and on average there was only one infected *A. gambiae* in every 14th room in 18 months ; this would mean that only one person in 56 would receive an infective bite in the same period. A figure illustrates the enormous reduction that has taken place in the parasite rate of children during this period, and even among those who became infected the author thinks that most did so when they were outside the controlled area, and gives reasons for his opinion. The number of parasites in the blood of infants increases with age up to 2–3 years, as does the number infected ; thereafter both decline. Comparison with malaria incidence outside the controlled area, and in Freetown as recorded in 1931, shows that great reduction has been effected.

WALTON (p. 1062) has been able to correlate the number of infective bites received each year by children in Freetown, with the parasite rate. He makes the point that reduction of parasite rate to 5 per cent., usually considered a satisfactory result of control, may reduce the children's immunity without any appreciable reduction of the disease. In comment TREDRE contests some possible implications of this view.

MACDONALD (p. 239) has written a long pamphlet on malaria control, for the benefit of laymen and medical men in India (particularly those connected with estates), in which he pays special attention to the new insecticides and drugs now available.

For the control of breeding of Indian anophelines which live in still water in association with various water plants, RAO and RAMAKRISHNA (p. 41) show that manual removal of the plants leads to overgrowth of algae, but that this can be avoided by planting the common aquatic herb *Ottelia alismoides*. The best prevention is the planting of vegetables on the beds of the tanks when they are dry in summer ; this seems to render the soil sterile when the water accumulates again.

NAGENDRA (p. 41) writes of the value of dry-leaf packing of streams for control of mosquito breeding.

A Committee of engineers and malariologists in India (p. 757) has laid down the principles which should be observed, in road and railway construction, so that the risk of malaria may be avoided.

The extensive and carefully planned system of malaria prevention which is now routine in the Tennessee Valley is discussed by BISHOP and HINMAN (p. 759). They point out that many of the engineering features which help to prevent the breeding of anophelines are built in at the stage of construction of the reservoirs. Water-level manipulation is now well understood, and together with shore-line maintenance and improvement, almost makes the use of larvicides unnecessary. These are sometimes needed, however, and DDT has supplanted paris green ; it is also used as residual spray in houses, where it gives better protection than routine gauze screening. A full account of malaria control on impounded water has been published by the United States Public Health Service and the Tennessee Valley Authority (p. 822)

GARTRELL and KIKER (p. 760) go into the detail of the engineering problems involved. The treatment of the reservoir margins in the Tennessee Valley involves two methods:—deepening and filling; diking and dewatering. Dewatering involves the use of pumps and recurring expenditure until the deepening and filling procedure is carried out. The subject is discussed by SIMMS and KIKER (p. 1061).

NEWBOLD and COCHRANE (p. 307) have devised an automatic siphon for antimalarial work, which has given good results in the West Indies. Details must be sought in the original.

PRATT (p. 977) has studied the plant communities of Porto Rico and their relation to the breeding of *A. albimanus* and other species; he discusses the control measures suitable for the various conditions.

GRAY (p. 309) has written an account of some of the important mosquitoes of Japan, and of methods of control.

Malaria in Malaya is described in a book by SANDOSHAM (p. 1045), who has paid attention to control, but in the period before DDT, and the latest drugs, were available.

Insecticidal methods.—MISSIROLI (p. 151) gives an account of the campaign undertaken against mosquitoes in Italy, where reliance has been placed on spray-painting of houses with DDT. The figures quoted show striking reduction of mosquitoes, of cases of malaria, and of deaths from malaria and from all causes. The reduction in deaths from all causes is probably a result of the reduction of enteric diseases consequent upon the wide destruction of house flies achieved by DDT.

AZIZ (p. 152) gives a detailed account of the work done during 1946 in the *Anopheles*-eradication scheme for Cyprus. Only part of the island was attempted in that year, but the work is to be extended later. DDT in oil was used as a larvicide, and as a residual spray in houses; pyrethrum was also used. The results were satisfactory though complete eradication was not achieved in this first year. The local anophelines are described.

The enormous control scheme undertaken in Greece in 1946, with DDT, is described by VINE (p. 492). For hibernating mosquitoes residual spraying was practised with a 5 per cent. DDT at 220 mgm. per square foot, and for larvicidal work also 5 per cent. DDT was used. Aircraft were used for marshes. These applications were made time after time from spring to autumn, and although comprehensive statistical data are not available, the amount of malaria was much less than the expected amount, some 80 per cent. of the population at risk having been protected. In addition, flies and sandflies almost disappeared, but bees were little affected after blossom time. The effects of DDT on the 6,000 labourers were negligible.

LIVADAS *et al.* (p. 758) report on a special investigation they made to assess the results of this programme. They found spleen rates reduced to half the previous figures and parasite rates to one tenth; in unprotected areas the parasite rate had not declined.

LIVADAS (p. 758) describes the campaign of the following year, when by house-spraying and larvicidal methods, all with DDT, over 4 million people were protected. The mosquitoes were again controlled, but the house flies much less so.

A big programme of house spraying with DDT in the Veneto Provinces of Italy was followed by a great reduction in malaria (SEPULCRI, p. 758).

BERBERIAN (p. 870) has used 5 per cent. DDT in kerosene with success as a residual spray and as a larvicide, in Lebanon where the vectors are *A. sacharovi* and *A. superpictus*.

AFRIDI and BHATIA (p. 493) have used DDT as a residual spray near Quetta, India, with success. At a concentration of 25–38 mgm. per square foot there

was apparently a reduction in the incidence of malaria; the anophelines concerned were *A. superpictus*, *A. culicifacies* and *A. stephensi*.

PURI *et al.* (p. 154) have published four useful papers, in which they show the value of DDT in oil or turpentine as a larvicide in ricefields, pits and streams, and as a residual spray (especially against *A. minimus* and *A. superpictus* in Bengal and Baluchistan respectively). They give details of amounts used.

In an investigation of the effect of spray treatment of African houses with pyrethrum or DDT in kerosene, Muirhead THOMSON (p. 405) has shown that though the numbers of *A. gambiae* and *A. melas* caught in houses after treatment is reduced, this is rather due to the fact that they are driven to rest outside after feeding, even more than they normally do. Low house catches, therefore, do not necessarily indicate heavy mortality or reduction of biting activity; these mosquitoes still seek human blood, but they do not normally rest much within the houses, and a heavy dose of kerosene on the walls has a repellent effect.

In field trials in Sierra Leone, DAVIDSON (p. 157) has demonstrated that Gammexane (0·5 per cent. solution at 10 mgm. per square foot of surface) used as a residual spray, is very effective in reducing for 6 months the mosquito population in houses (*A. gambiae*, *A. melas*, *A. funestus*). He found, however, (p. 158) that in the group of villages sprayed there was little change in the malaria rate as a result of these measures.

TONKING *et al.* (p. 241) conducted a campaign of residual DDT spray in a malarious district of Mauritius where *A. funestus* is the chief vector. They demonstrated great reduction in the numbers of *A. funestus* caught in the sprayed houses, after 3 treatments of 178, 112 and 150 mgm. DDT per square foot, and they found some reduction in the parasite rate of the people.

NAIR (p. 1063) reports marked reduction in the anopheline vectors (especially *A. letifer*) in a town in Malaya after DDT residual spray had been used three times in three months. The effect on spleen rates and parasite rates was also good.

WATERHOUSE and ATHERTON (p. 975) have tested pyrethrum and other sprays against various mosquitoes, including *A. punctulatus farauti*, and show that a spray containing 0·14 per cent. pyrethrins gives good knockdown. This was used by the Australian Army authorities until the advent of DDT, which was used to reinforce the pyrethrins in an all-purpose spray.

BANG *et al.* (p. 45) show that DDT residual spray at 100 mgm. per square foot was effective in reducing the numbers of *A. punctulatus farauti* and *A. subpictus* found in houses in villages of New Guinea; even after 4 months the numbers were only 5 per cent. of the numbers found in adjacent unsprayed villages.

YUST (p. 682) shows how effective a combined campaign of DDT residual spray and DDT in kerosene as a larvicide was against *A. farauti* in Espiritu Santo, New Hebrides, during the war.

MCCAULEY *et al.* (p. 760) have shown that for DDT to be effective against *A. quadrimaculatus* as a residual spray in houses it must be applied not only to likely mosquito resting places (undersides of furniture, etc.), but also to walls and ceilings as a whole.

FLETCHER and KRAUSE (p. 761) concentrated on using DDT spray on all houses and all likely outdoor resting places of *A. quadrimaculatus*, over a large area, in the hope that this might be more effective than residual spraying of houses combined with the use of field larvicides. The results obtained encouraged this hope, though eradication was not achieved.

BRADLEY and FRITZ (p. 42), as a result of a second season's residual DDT spray programme, found that at a concentration of 200 mgm. per square foot,

over 98 per cent. of houses (in southern U.S.A.) were free of *A. quadrimaculatus* 4 months or more later, and that fewer of the anophelines taken in sprayed houses showed evidence of human blood than of those taken elsewhere. In comment, GORDON refers to British work on *A. gambiae* which indicates that at least 200 mgm. per square foot are needed for effective results.

As a result of experience of treating with DDT emulsion the insides of all buildings in an area near the Wheeler Reservoir (Tennessee Valley) HINMAN and CUTKOMP (p. 156) conclude that this procedure offers better protection than mosquito-proofing against malaria transmission. *A. quadrimaculatus* is the mosquito concerned. CUTKOMP (p. 156) has compared the immediate and residual action of several insecticides, but for details the original should be consulted.

WEATHERSBEE *et al.* (p. 1063) have observed that at concentrations of DDT of 40 mgm. per square foot to animal houses the surface remained free of *A. quadrimaculatus* for 27 days ; at 200 mgm. the period was 135 days.

LINK (p. 43) has made blood surveys in South Carolina, and also in Porto Rico, on populations in areas where residual DDT spray was used, and on control populations. The vectors were *A. quadrimaculatus* and *A. albimanus* respectively, and the results indicated a reduction in malaria, but the doses of DDT are not given.

A description of the malaria situation of British Guiana, and of the breeding habits of *A. darlingi* the chief vector, is given by STAGE and GIGLIOLI (p. 308), who show that DDT applied as a residual insecticide is most effective against this mosquito. GIGLIOLI (p. 976) states that in the parts of British Guiana in which DDT residual spray has been extensively used, *A. darlingi* has been eradicated. The aim is to treat all buildings with 150 mgm. DDT per square foot at intervals of 8 months or even longer.

As a result of their experiments GALVÃO and DAMASCENO (p. 683) think that application of DDT (195 mgm. per square foot) as a residual insecticide in wooden houses at intervals of 4 months should be effective against *A. darlingi* where breeding takes place throughout the year.

A DDT spray campaign against *A. darlingi* in Brazil was very effective in reducing the number of mosquitoes in the houses, and the number of cases of malaria (BRAGA *et al.*, p. 408).

The use of DDT as a residual spray was apparently successful in reducing the incidence of malaria along the coast of Peru (CORRADETTI, p. 871).

KUCHER (p. 307) writes of a Russian insecticide derived from coal tar.

Larvicidal methods.—Experiments in England by JOHNSON and WALTON (p. 306) showed that the critical density of application of DDT for the control of anopheline larvae is about 40 gm. per acre (10 mgm. per square metre), below which results are unreliable, especially if there are reeds. Oil solution is better than emulsion.

JOHNSON and GOODMAN (p. 45) show that DDT in oil, with a spreading agent, gives satisfactory results against larvae of *A. quadrimaculatus* at the rate of 75 gm. DDT per acre. The amount of oil needed is very much less than when oil without DDT is used.

In an enquiry on the effect of DDT (used as a larvicide) on wild life, TARZWELL *et al.* (p. 46) show that at 0·1 lb. per acre it had considerable effect on insects, at 0·4 lb. an effect on fish, but not much on birds, rats, rabbits, etc., or on plankton.

DEONIER *et al.* (p. 581) have produced some experimental evidence that DDT applied to mud is effective against mosquito larvae which appear after subsequent flooding.

SAUTET *et al.* (p. 45) have obtained very fine suspensions of DDT by treating with supersonic waves the emulsions of benzene solutions mixed with water.

PUTNAM and HACKETT (p. 152) give an account of the antimalaria work done in Albania from 1929 to 1938, when drainage or filling of swamps, training of streams, alterations of salinity, and paris green, were the means used for control. They describe the habits of the common vectors.

DE MEILLON and THORP (p. 149) have noted that quinine and mepacrine will inhibit the growth of larvae of *Aëdes aegypti*, but that this inhibition is reversed if brewer's yeast is added in quantity to the medium.

Malaria of Birds

Sporozoites of *P. gallinaceum* from mosquitoes which have been ground up in saline or Ringer solution are soon harmed if kept at 24°C., and still sooner at 37°C., but TONKIN (p. 243) has shown that in plasma or plasma saline they survive with no apparent change, for more than 14 hours.

WHITMAN (p. 1065) has been able to preserve sporozoites of *P. gallinaceum* for 72 hours by suspending them in an extract of washed chicken erythrocytes. This is an important step in experimental work.

LEWERT (p. 582) has grown *P. gallinaceum* in tissue culture, and has observed that subinoculation into chicks led to exclusively exoerythrocytic infection.

GRAMICCIA and BLACK (p. 685) cultivated *P. gallinaceum* in tissue culture, from birds which had been infected by blood inoculations of trophozoites, not by sporozoites ; typical exoerythrocytic forms were found in macrophage-like cells.

MARSHALL (p. 495) discusses the glucose metabolism of *P. gallinaceum* and the action of antimalarial agents on it. Details should be sought in the original.

The technique of rearing and feeding *Aëdes aegypti* used for transmission of *P. gallinaceum* is described in detail by JOHNSON (p. 309).

HAAS and AKINS (p. 310) have succeeded in transmitting *P. gallinaceum* by *A. quadrimaculatus* ; this has not previously been done.

Quinine and paludrine, administered to *Aëdes aegypti* by allowing them to feed before and after infection on sugar solution containing the drugs, were shown by JOHNSON and AKINS (p. 1065) to exercise marked inhibitory action on the development of sporozoites of *P. gallinaceum*.

WHITMAN (p. 872) has shown that the hydronaphthoquinone M 2279 has some effect on oöcyst formation if ingested by *Aëdes aegypti* within 48 hours of an infective feed of blood containing *P. gallinaceum*. It has no effect on sporozoites. CLARKE and THEILER (p. 686) have experimented with a hydroxynaphthoquinone in *P. gallinaceum* infections. It is very active against the earliest phases of the developing parasite and there is strong evidence that the effect is against the sporozoite itself ; complete prophylaxis could be obtained. It is also active against late exoerythrocytic forms, and against blood forms.

TONKIN and HAWKING (p. 243) have studied the technique of testing drugs on *P. gallinaceum* ; for sulphadiazine the best results were obtained when the drug was administered over a period of 4 days.

TERZIAN (p. 767) describes his method of using *Aëdes aegypti* and *P. gallinaceum* in experiments to determine the antimalarial activity of various drugs.

PARAENSE (p. 47) reports his experiments with *P. gallinaceum* infection of chicks, induced by either sporozoite inoculation or blood inoculation. Details are given in the original abstract. Treatment with quinine did not eliminate all trophozoites, and exoerythrocytic forms were found in birds so treated ; moreover, it seems that the blood trophozoites increased as a result of increase of the exoerythrocytic forms. Only the blood forms seem to stimulate immunity.

KNOPPERS (p. 158) has found some slight resistance to quinine in *P. gallinaceum* in chickens treated with small doses.

Williamson and Lourie (p. 48) give details of their experiments which showed that resistance to paludrine developed in *P. gallinaceum* (as a result, probably, of mutation) in chicks treated with that drug in two schedules, but that resistance to quinine, mepacrine, M 3349 or sulphadiazine could not be provoked.

Bishop and Birkett (p. 1066) in comparable tests on *P. gallinaceum* in chickens, showed that with relatively small doses of the various drugs there was no development of drug resistance to mepacrine, only slight to pamaquin, but 40-fold increase to paludrine. This resistance to paludrine persisted on subinoculation.

Piekarski (p. 1067), similarly, failed to produce resistance to mepacrine.

Exposure of chicks infected with *P. gallinaceum* to atmospheres containing excess of oxygen did not benefit them (Terzian and Saxe, p. 496).

Trager (p. 159) discusses the relation of biotin and a fat-soluble substance having the same properties, and found in plasma, to the course of avian malaria; details should be sought in the original.

Taliaferro and Taliaferro (p. 768) show that nitrogen mustard, which is toxic to lymphocytes, has a decided action in damaging the parasiticidal mechanism of acquired immunity when administered to chickens either shortly before or shortly after infection with *P. gallinaceum* or *P. lophurae*.

Kikuth and Mudrow (p. 47), in a paper published in 1939, discuss the early stages of *P. cathemerium* development after injection of sporozoites.

Simpson (p. 873) has studied the cycle and course of *P. cathemerium* infections in ducks and canaries.

Beckman (p. 1067) has shown that if sporozoites of *P. cathemerium* are incubated with canary blood and hen blood, the latter exerts a strong inhibitory action on them, preventing infection of birds subsequently injected, whereas the canary blood has no similar action.

Walker *et al.* (p. 687) describe the technique they adopted during the war for testing drugs against *P. cathemerium*; for details the original should be consulted.

Walker and Richardson (p. 688) discuss the synergic effects observed, in *P. cathemerium* infections, between the 8-aminoquinolines (plasmoquine, pentaquine) and certain naphthoquinones. These effects were evident in curative treatment, but much less so in suppressive treatment, which suggests differences in the mechanism of the two processes.

Gingrich (p. 980) found a progressive decline in the immunity acquired by canaries after infection with *P. cathemerium* by injections of blood, and cured by drugs. Immunity had disappeared completely in 8 months.

Redmond (p. 769) has studied the electric charge of red blood cells in *P. relictum* infections of pigeons.

Micks (p. 497) shows that two strains of *P. elongatum* lost the power to produce gametocytes, one had been passed through ducks, the other through canaries.

Thompson *et al.* (p. 1066) show that injected radio-active iron has no effect on *P. lophurae* in ducks or *P. cathemerium* in canaries.

Rigdon (p. 49) thinks that accumulation of CO_2 in the body at the peak of infection may be the cause of the sudden fall in number of parasites after the crisis. In comment, Garnham remarks that the experiments quoted (with *P. lophurae*) are not entirely convincing.

Rigdon and McCain (p. 409) discuss some of the factors which influence the degree of parasitaemia in ducks infected with *P. lophurae*, especially the oxygen and CO_2 content of the blood. Details should be sought in the original.

Rigdon and Rostorfer (p. 979) consider that the anaemia caused by *P. lophurae* in ducks is due to destruction of mature erythrocytes and their replacement by the less efficient erythroblasts. The latter are not well suited to the needs of the parasites.

TONKIN and HAWKING (p. 409) describe exoerythrocytic forms of *P. lophurae* grown in tissue culture of turkey liver.

THOMSON *et al.* (p. 49) have found it possible to immunize ducks with *P. lophurae* or *P. cathemerium*, killed by formalin, injected intramuscularly in a medium of paraffin oil with killed tubercle bacilli and an emulsifying agent. Repeated injections protect for about 6 months; the vaccine prevents death and reduces parasitaemia.

HAIBA (p. 769) records the plasmodia found in common Egyptian birds.

Malaria of other Animals

The physiological changes in the blood of monkeys infected with *P. knowlesi* are described by OVERMAN and FELDMAN (p. 766). In the stage of heavy infection the red cells are reduced in number and carry little oxygen; tissue anoxia results and is the cause of death.

FREUND *et al.* (p. 766) have succeeded in inducing a considerable degree of immunity in monkeys by injecting a vaccine of *P. knowlesi*, with certain adjuvants.

Soluble antigens from *P. knowlesi* and *P. lophurae* have been used for complement-fixation tests; the former was useful in homologous infections only, the latter in both (DAVIS, p. 767).

HUFF and COULSTON (p. 762) record their attempts to find, without success, pre-erythrocytic stages of *P. vivax* and *P. cynomolgi*.

RODHAIN (p. 978) has shown that *P. rodhaini* of the chimpanzee is transmissible to man, and *P. malariae* to the chimpanzee. In comment, GARNHAM remarks that the two should be regarded as identical.

VINCKE and LIPS (p. 979) describe *P. berghei*, a new species from a rodent in the Belgian Congo.

The developmental cycle of *Hepatocystes kochi* in the monkey has been worked out and described by GARNHAM (p. 683). Details should be sought in the original.

Charles Wilcocks

MALARIA

DOELEMAN, H. & VAN THIEL, P. H. L'épidémie du paludisme à Middelbourg dans les années 1940 à 1946 y compris un examen de porteurs de parasites. [**Malaria Epidemic in Middelbourg 1940 to 1946, including an Examination of Parasite Carriers.**] *Bull. Soc. Path. Exot.* 1948, v. 41, Nos. 9/10, 580–84.

It was in 1900 that malaria was first proved to be present in Zeeland in the Netherlands. There were 200 primary infections in that year. Thereafter the disease disappeared from the province till 1920–1924, when fresh outbreaks occurred. In 1939 sporadic cases still occurred, the precursors of an epidemic which commenced in 1940 with 40 cases. Maximum prevalence was in 1943, with 300 primary cases. The epidemic ceased in 1945, when only 14 cases occurred.

The malaria outbreaks in Middelbourg differed in certain respects from those occurring in other parts of the Netherlands. The maximum prevalence was in August, sometimes in July, but never in May–June: most cases were single cases, even when these occurred in households with many children; the disease was not specially prevalent among children.

The spleen index among school children was remarkably low, 3·2 per cent. During this examination, only one case was discovered that had not previously been notified by local doctors. In September 1941, cellars in the middle of

Middelbourg, that had been exposed by the bombardment of the town in May 1940, were found to be prolific breeding places of *A. maculipennis atroparvus*. It is remarkable that this biotype should have selected such freshwater breeding places, some of them shaded from sunlight, when saline breeding places were readily accessible in the neighbourhood. The extension of malaria had already begun when this unusual source of supply of the anopheline vector first became operative.

Control measures included (1) administration of quinine (1 gm. for adults) on each of two successive days each week, from mid-August to the end of October, to all persons who had suffered from malaria during that or the preceding year, with special attention to the known 65 parasite carriers : (2) spraying the bedrooms of these persons every 15 days with shelltox, during the same period of time ; (3) the abolition of mosquito breeding places in the cellars of the town.

One of the reasons why Middelbourg alone, and no other part of Zeeland, suffered from the epidemic was the arrival of infected persons. The barracks were occupied by German troops ; many horses were stabled in the middle of the town and attracted large numbers of anophelines.

The final extinction of malaria was probably accelerated by the inundation in October 1944 : in the summer of 1945 practically the whole island was under sea-water. No mosquito breeding places were left. There was not a single fresh infection of malaria in Middelbourg in either 1946 or 1947.

Norman White

Jaujou, C. & Toumanoff, C. Compte rendu d'un sondage malariologique effectué en Corse (16–30 Août 1947). [**Cursory Malarial Survey in Corsica.**] *Bull. Inst. Nat. Hyg.* Paris. 1948, July–Sept., v. 3, No. 3, 468–81.

A visit of two weeks duration was paid by the authors to Corsica to enable them to obtain preliminary information as to the extent to which war-time events, including the temporary cessation of antimalarial work, had influenced the malaria endemicity of the Island. The inspection was made in the latter half of August, 1947. Visits were paid to a few localities in both the eastern and western sides of the Island.

Spleen and parasite rates of the few places visited were on the east coast 12·8 and 48·6 per cent., and on the west coast 9·6 and 32·2 per cent. There was evidence of locally acquired malaria in Ajaccio, a town which was formerly considered to be almost free from malaria. Gamete carriers were relatively numerous. *A. maculipennis labranchiae* and *A. sacharovi* were found on both sides of the Island. One infected *A.m.labranchiae* was captured. A further more detailed survey was to be carried out in the late autumn.

Norman White

Buonomini, G., Sicca, G. T. & Manfredi, M. La malaria all'isola d'Elba. [**Malaria in the Island of Elba.**] *Riv. Italiana d'Igiene.* 1948, Jan.–Feb., v. 8, Nos. 1/2, 1–12, 1 map & 1 chart.

Between the world wars, malaria was a disease of little account in the Isle of Elba. After the first war, a considerable outbreak occurred in connexion with constructional work on a cement factory ; this rapidly subsided. In 1943, there was a noteworthy increase in malaria prevalence and the incidence increased in the following years. The Commune of Portoferraio in the north of the Island was chiefly affected. This exacerbation of the disease was attributed in part to the return of soldiers from infected war zones, the arrival of troops from Corsica and Sardinia, and passage of Moroccan troops through the Island. The authors

were invited to study the situation and carried out an investigation that lasted from September 1946 to October 1947. Their findings are summarized in this report.

The only anopheline found was *A. maculipennis labranchiae*. This marks the northern-most limit in Italy of the distribution area of this sub-species. Its areas of distribution in the Island are circumscribed ; breeding places are not numerous, and prevalence is not excessive.

Malaria cases occurring in 1946 and 1947 are given in graphic form. All were *P. vivax* infections. Cases occurring in February and March were presumably infections contracted in the previous autumn. There is a steep rise in the curve which reached its height in July or August. Spleen rates of children were indicative of low endemicity.

A DDT campaign was started in June 1947. All houses, stables and out-buildings in the infected areas were sprayed. This appears to have cut short the epidemic, but *labranchiae* was still found breeding in limited numbers. Antilarval measures were then superimposed. The measures were to be continued the following year and it was hoped that they would be successful in eradicating *Anopheles* and malaria from the Island. *Norman White*

Foy, H., Kondi, Athena, Damkas, C., Depanian, Margaret, Lefcopoulou, Theresa, Bach, L. G., Dax, R., Pitchford, J., Shiele, Pamela & Langton, Moira. **Malaria and Blackwater Fever in Macedonia and Thrace in relation to DDT.** *Ann. Trop. Med. & Parasit.* 1948, Sept., v. 42, No. 2, 153–72, 5 figs. & 1 map. [21 refs.]

This is a record of a malaria survey carried out in Macedonia and Thrace during November and December 1946 to assess the relative causative effects of the nation-wide DDT campaign of the preceding year and of natural variation in malaria endemicity, respectively, on the low malaria-rates in northern Greece since the severe malaria epidemic of 1942. The incidence of malaria in Macedonia has long been characterized by annual variations in intensity, probably connected with variations in anopheline density which is dependent on the rainfall in late winter and spring.

During the twenty-four years 1923–46 there was a noteworthy overall decline in malaria morbidity in Macedonia, punctuated by occasional years of abnormal prevalence. As a measure of malaria incidence, the authors use the percentage of malaria in total admissions to the Central Refugee Hospital and the Municipal Hospital in Salonika, the former of which is mainly occupied with rural populations. The mean malaria incidence for the twelve-year period 1923–34 was 17·5 per cent. ; for 1935–46 it was 10·6 per cent. In 1942 there was a major malaria epidemic that affected the whole of Greece. The incidence in Macedonia rose from 12·2 per cent. in 1941 to 28·4 per cent. in 1942. This epidemic occurred during the German occupation when there was much disorganization and acute food shortage. There was a rapid decline in malaria incidence in the following years : in 1945 it was only 3·3 per cent. The extensive use of atebrin [mepacrine] may have contributed to this decline. The DDT campaign was undertaken late in 1945.

A country-wide survey of Macedonia and Thrace was carried out during November and December 1946 : 12,000 spleens were palpated and the blood of 7,000 school children, and of 2,200 infants who had lived through only one transmission season was examined. The parasite-spleen ratio which in the past had usually ranged from 1 : 2 to 1 : 4 had fallen to 1 : 30 to 1 : 70. No evidence wa obtained that DDT had contributed much to the remarkable reduction of malaria incidence in Macedonia and Thrace. The incidence in 1946 was only 1·7 per cent.

The greatly increased incidence of malaria in 1942 was not accompanied by a corresponding increase in the incidence of blackwater fever. *Norman White*

Montalvan C., J. A. Paludismo en Guayaquil. [**Malaria in Guayaquil.**] *Rev. Ecuatoriana de Hig. y Med. Trop.* Guayaquil. 1944, Apr., v. 1, No. 2, 131–60, 2 maps, 5 graphs & 1 fig.

Huff, C. G. **Exoerythrocytic Stages of Malarial Parasites.** *Amer. J. Trop Med.* 1948, July, v. 28, No. 4, 527–31. [19 refs.]

This is an account of the various questions relating to the exoerythrocytic stages of malaria parasites. It was written before the demonstration of the hitherto hypothetical exoerythrocytic stages in mammalian malaria.

The points dealt with, which need not now be elaborated further, are :—

" What are exoerythrocytic stages ? "

" Why were they so long in being discovered ? "

" What types of exoerythrocytic stages are known ? "

" In what species have exoerythrocytic stages been demonstrated ? "

" What about the claims for finding exoerythrocytic stages in human and simian malaria ? "

" Do such stages really exist in human or simian malarial infections ? "

" Do exoerythrocytic stages offer the means for any new approaches to old problems in malaria ? "

" What is the significance of the exoerythrocytic stages in the life-cycle ? "

H. E. Shortt

Bijlmer, J. & Kraan, H. **Is the Gametocyte Production of *Plasmodium vivax* influenced by Elimination of the Mosquito Passage ?** *J. Trop. Med. & Hyg.* 1948, Nov., v. 51, No. 11, 222–5.

If *Plasmodium vivax* infection is transmitted serially by blood inoculation, the sexual cycle is eliminated and it is conceivable that the formation of gametocytes may decline or even cease. Some observations appearing to substantiate this effect have, in fact, been disproved when subjected to critical tests.

The authors investigated the problem at the Wilhelmina Hospital in Amsterdam and arrived at the following conclusions :—

(*a*) The ability to produce many or few gametocytes is a strain characteristic in a given plasmodial species.

(*b*) In malaria, exclusively transmitted by blood inoculation, there occurs a diminished power of the parasite to produce gametocytes. The decline, in extent and rapidity of onset, varies with the strain in use. *H. E. Shortt*

Gaud, J. Fréquence au Maroc et rôle vecteur possible d'*Anopheles sergenti*, Theo. [**Frequency and Possible Vector Rôle of *Anopheles sergenti* in Morocco.**] *Bull. Soc. Path. Exot.* 1948, v. 41, Nos. 7/8, 498–501, 1 map & 1 fig.

During an anopheline survey of Morocco in 1947, the following species were found as larvae and adults : *A. maculipennis* [the subspecies is not stated, but it is presumably *labranchiae*], *A. sergenti*, which was surprisingly abundant, *A. turkhudi* (*? A. hispaniola*), *A. multicolor* and *A. claviger* ; all these were house frequenters in different degrees. Other species taken were *A. marteri* (a new record for Morocco) and *A. coustani* from some new localities.

The distribution of *A. sergenti* is indicated on a sketch map, showing that it occurs near the coast as well as inland. The highest altitude at which it was captured was 1,700 metres (approx. 5,500 feet). It was prevalent between June and November and most abundant in September and October. Its relationship to malaria transmission is uncertain ; 35 dissections were negative, proving nothing ; but this species enters houses readily and after *A. maculipennis* is the most domestic anopheline.

The wings of the Moroccan form of *A. sergenti* differ from the typical form in that the basal and preapical dark areas of the costa are so extended that in some specimens the two adjacent pale spots are obliterated, leaving only two pale costal spots. *H. S. Leeson*

CAUBET, P., ABONNENC, E., RENÉ-BOISNEUF, P. & LOUIS-SIDNEY. Les moustiques du genre Anophelès à la Martinique. [**Anopheline Mosquitoes in Martinique.**] *Arch. Inst. Pasteur de la Martinique.* 1948, Jan., v. 1, No. 1, 9–11.

Between November 1946 and November 1947, the authors collected 3,303 larvae and pupae of *Anopheles aquasalis* and 22 larvae and pupae of *A. argyritarsis* in Martinique. They give the names of the localities and the types of breeding places from which they obtained them and note that *A. albimanus* was not seen. *H. S. Leeson*

BURGESS, R. W. **The Experimental Hybridization of** *Anopheles quadrimaculatus* **Say and** *Anopheles maculipennis freeborni* **Aitken.** *Amer. J. Hyg.* 1948, Sept., v. 48, No. 2, 171–2.

" Hybridization between *Anopheles quadrimaculatus* Say and *Anopheles maculipennis freeborni* Aitken under laboratory conditions is reported.

" *A. quadrimaculatus* males mated with *A. maculipennis freeborni* females produced 30·3 per cent. fertile ova. The fertility of the opposite cross was only 2·0 per cent.

" All larvae were small and weak, and none survived beyond the third instar."

PRATT, H. D. **Influence of the Moon on Light Trap Collections of** *Anopheles albimanus* **in Puerto Rico.** *J. National Malaria Soc.* 1948, Sept., v. 7, No. 3, 212–20, 6 figs.

Four years' trapping records and observations on *Anopheles albimanus* are discussed in this paper. Charts are presented to illustrate the effect of moonlight on the catches in light traps.

Experiments with light traps of different light intensity showed that they attracted *A. albimanus* in numbers which varied according to the intensity of the light given out by the traps. When a single trap was used, the size of the collection varied with the " dark " and " bright " phases of the moon ; the darker the night the greater the numbers of mosquitoes attracted. When an animal trap was situated near a light trap the light collections were often higher than those in the bait trap during the " dark " phase of the lunar cycle and approximately equal to, or lower than, those in the animal trap during the " bright " phase. The size of the collections from both types of traps fluctuated seasonally, but those from the light traps were also subject to cyclic fluctuations within each month. The suggestion is made that the mosquitoes do not see the light trap so well during the " bright " phase of the moon as during the " dark " phase. Animal traps may therefore give a truer conception of the trends in anopheline populations.

It is more difficult to determine an index for " satisfactory control " based on light trap collections alone, but it may be stated that, in general, little or no malaria transmission occurred when light catches averaged 1–5 *A. albimanus* per night during the " bright phases " and 5–20 during the " dark phases " of the moon. These figures are comparable with the single figure of 2 to 5 *A. albimanus* per animal trap per night given as the " satisfactory control " figure for military bases. *H. S. Leeson*

Deane, L. M., Causey, O. R. & Deane, M. P. Notas sôbre a distribuição e a biologia dos Anofelinos das regiões Nordestina e Amazônica do Brasil. [**Notes on the Distribution and Biology of the Anopheles of the North-East and Amazon Regions of Brazil.**] *Rev. Serviço Especial de Saúde Pública.* Rio de Janeiro. 1948, May, v. 1, No. 4, 827–965, 6 graphs & 39 maps on 6 pls. [34 refs.] English summary.

The observations recorded in this paper were made by the authors from 1939 to 1944. Many thousands of anopheline mosquitoes, larvae and eggs were examined and thirty-six species were found. A number of identifications were confirmed by laboratory-bred specimens. The distribution of each species is given in tables and shown on maps. Other tables show the results of salivary gland and stomach dissections for malaria infections ; the results of hourly collections and collections in animal shelters and human dwellings are also given. The results of hourly captures of *Anopheles darlingi*, *A. albitarsis* and *A. aquasalis*, both indoors and outside, are shown on six graphs.

A. darlingi and *A. aquasalis* are the only species of real importance in the transmission of malaria in these regions ; the African invader *A. gambiae* has been eradicated.

A. darlingi is the most domestic species ; and previous observations that this anopheline normally enters houses during the late hours of the night were confirmed, though two peaks of entry, one at sunset and one just before sunrise, were often noted. Where the species was abundant, it was captured feeding outside as well as indoors at any time, even during the hottest part of the day ; but where it was rare it could only be found indoors during the late hours of the night or at dawn. Comparative captures yielded larger numbers on horse than on man, indicating that this species is perhaps less anthropophilic than it was thought to be. Among 1,600 dissections of females of *A. darlingi* 28 (1·8 per cent.) were found to be infected, though for different localities the rates varied from 0 to 50 per cent. Where the species was abundant the infection rate was low and the opposite was also true.

Whereas *A. darlingi* is a freshwater breeder, *A. aquasalis* larvae were usually found in brackish water, both along the coast and as far inland as 140 kilometres from the sea. *A. aquasalis* invades houses and feeds readily on man in the north-east of the country but in the coastal areas of the Amazon region it is far less domestic. It is a malaria vector, either alone or together with *A. darlingi*, but in the areas investigated it is not so important as *A. darlingi*, because it is less domestic in habit, and because it is dangerous only when abundant.

Two forms of *A. albitarsis* were encountered. One of them (var. *domesticus*) was found feeding frequently on man during a malaria epidemic in an area where it was the only abundant anopheline ; in other places *A. darlingi* and *A. aquasalis* were also present. The other form [not named] feeds on animals and does not seem to take any part in the transmission of malaria.

One other anopheline, *A. pessoai*, (perhaps synonymous with *A. brasiliensis*) was once found infected with sporozoites. There is no evidence that any of the other species is a natural vector of malaria in these regions. *H. S. Leeson*

PITTENDRIGH, C. S. **The Bromeliad-Anopheles-Malaria Complex in Trinidad. I. The Bromeliad Flora.** Reprinted from *Evolution*. 1948, Mar., v. 2, No. 1, 58–89, 7 figs. (4 on pls.). [27 refs.]

The Anopheline mosquitoes of the subgenus *Kerteszia* breed in water held among the leaf bases of Bromeliad plants, growing as epiphytes on trees in Tropical America. The present paper is a contribution to the natural history of these plants, of which fifteen genera and a large number of species are found in Trinidad. The author has produced an interesting classification of the types of environment which they inhabit. Some grow on rocks and root in soil: others have developed "nutritive independence": they grow on limbs of trees, hold water and humus among their leaf bases and exploit these materials. The distribution of species is determined rather by light than by atmospheric moisture. *P. A. Buxton*

MARTINEZ MUJICA, Celia. Reticulo endoteliosis paludica. [**The Reticulo-endothelial System in Malaria.**] *Medicina*. Mexico. 1948, Oct., 10 & 25, Nov. 10 & 25, v. 28, Nos. 565, 566, 567 & 568; 417–26; 454–7; 459–79; 481–8, 10 figs. [Numerous refs.]

This article deals fairly exhaustively with the reticulo-endothelial system, not only as regards malaria, but more generally. The whole consists of ten sections; but much of it is recapitulatory and brings together our knowledge of the subject and sums up the latest views on it, without contributing much that is really new; in fact, a good deal has already been incorporated in the textbooks.

Section I sketches briefly the history of our knowledge of the r.e.s. from the time of Ranvier's observations in 1890; section II describes the normal histology of the system in the blood-vessels, the spleen, lymphatic glands, bone-marrow, the connective tissues, lungs, liver, brain, etc. Next follows an account of the physiology of the system as regards malaria, phagocytosis, haematolysis, *i.e.* destruction of red and white corpuscles and platelets, and haemopoiesis, the development of immunity or, rather, the prevention of its development when the r.e.s. is blocked. In Section IV the pathology of the r.e.s. is considered in connexion with infective diseases in general—the taking up of organisms by the cells of the system. This is followed by a description of the part it plays in paludism, with photomicrographs showing cells of the capillaries blocked by parasites, and of the spleen and liver in malaria and of the exoerythrocytic forms of *P. cathemerium* and *P. circumflexum* in the canary. There is presented a very clear schematic presentation of the parasitic cycle—the exoerythrocytic cycle, the cryptozoites of Huff; the schizogonic cycle of Golgi, and the sporogonic cycle of Ross [so named by the author]. Section VI treats of the r.e.s. and the clinical manifestations of malaria and states that the anaemia associated with the disease is not due solely to destruction of red corpuscles, but also to blocking and injury to the haemopoietic organs. Section VII discusses the rôle of the r.e.s. in malaria immunity, especially in the spleen, liver and bone-marrow, by causing concentration of histiocytes and hyperplasia of them and in stimulating phagocytosis by them. Next follow remarks on the laboratory diagnosis in regard to the r.e.s., indicating that the ordinary methods are inadequate to demonstrate "malarial reticulo-endotheliosis" and necessitating the reactions of Henry and Soberón. The epidemiology of malaria and its relations with the r.e.s. are evidenced (Section IX) by the splenic and parasitic indices. Finally, the subject of treatment is considered and it is shown that parasites not destroyed in the blood find refuge in the cells of the r.e.s., where they continue to develop and remain until conditions become

favourable, when they are discharged into the blood-stream, attack fresh corpuscles and set up a relapse. At present, says the author, we lack drugs which will attack the reticulo-endothelial phase of the parasite, but experiments are being undertaken to produce synthetically some product which will effect this. In conclusion, it is recommended that " malarial reticulo-endotheliosis should be investigated by all possible means, including the reactions of Henry and Soberón, in persons exhibiting mental disturbance of sudden onset who suffer or have suffered, from malaria, or who reside in, or have come from, malarious districts, if no other, obvious, cause for the disturbance can be found."

H. Harold Scott

Lippi, M. L'attività secretoria dello stomaco nella malaria cronica. [**Secretory Activity of the Stomach in Chronic Malaria.**] *Acta Med. Italica.* 1948, Sept., v. 3, No. 9, 231–4. English summary (10 lines).

This paper concerns twenty patients suffering from chronic malaria, all of whom had enlargement of the spleen and liver, well marked hypochromic anaemia and leucopenia. In each case a tube was introduced into the stomach in the early morning after the night's fast and left *in situ* till four samples of the gastric secretion had been obtained, at intervals of half an hour. In all samples there was a noteworthy decrease of total acidity and of hydrochloric acid content. This the author attributes to the changes in the blood, bone-marrow, liver and spleen that characterize chronic malaria. He thinks, too, that splenic hyperfunction may inhibit thyroid stimulation of the gastric secretion.

Norman White

Montalvan C., J. A. Algunas consideraciones sobre el diagnostico clinico del paludismo en comparación al resultado del examen de sangre. [**The Clinical Diagnosis of Malaria compared with Examination of Blood Films.**] *Rev. Ecuatoriana de Hig. y Med. Trop.* Guayaquil. 1944, Apr., v. 1, No. 2, 161–6, 2 figs.

Zaki, A. **The Value of Tyrosine Index in Malaria and other Endemic Diseases in Egypt.** *J. Roy. Egyptian Med. Ass.* 1944, Aug., v. 27, No. 8, 243–50. [Recd 13 Dec., 1948.]

" 1. The tyrosine serum index in pure cases of malaria is not always increased.

" 2. Other parasitic diseases increase the tyrosine index especially S. mansoni infection. The index was also definitely increased in cases of hypertension and pellagra.

" 3. It is very difficult to find pure cases of malaria in Egypt as the great majority of the rural population are very often infected with parasitic diseases and therefore tyrosine cannot be relied upon in the diagnosis of malaria."

Ciuca, M., Ballif, L., Chelaresco, M., Constantinesco, C. & Timişescu, A. Recherches comparées sur l'infection expérimentale, en but de malariathérapie, des malades appartenant respectivement à une région non paludéenne (Bucovine) et à une région endémique (Moldavie). [**Comparative Study of Infection as a Result of Malaria Therapy of Patients from a Non-Malarial (Bukavina) and a Malarial (Moldavia) Region.**] *Arch. Roumaines Path. Expér. et Microbiol.* 1945–1946–1947, v. 14, Nos. 1/4, 193–206, 10 charts.

This short paper makes some interesting comparisons between the relative susceptibility to the same strains of malaria of two populations in Roumania, one from an endemic area, Socola in Moldavia and the other form a non-endemic area, Bukovina. The patients reported on in these series were undergoing

treatment by therapeutic malaria and the data are strictly comparable as the malarial strains used were identical, *P. vivax* T. B. Hohr and *P. malariae* Q^R.

The results of the comparison showed that the patients from the non-endemic area had a markedly lower resistance to infection by these strains, as evidenced by the following findings : —

(*a*) They gave a hundred per cent. infection rate as compared with 83·1 per cent. in the case of those coming from the endemic area.

(*b*) The incubation period was shorter.

(*c*) The degree of parasitaemia was greater.

(*d*) Anti-malarial drugs took longer to cause disappearance of the parasitaemia, at least in the case of infection with *P. malariae*. *H. E. Shortt*

Ciuca, M., Ballif, L., Chelaresco, M. Vrabie, M. & Munteanu-Vasiliu, F. Particularités régionales de l'infection paludéenne utilisées en but de traitement (malariathérapie). [**Regional Factors affecting the Malarial Infection acquired as a Result of Malaria Therapy.**] *Arch. Roumaines Path. Expér. et Microbiol.* 1945–1946–1947, v. 14, Nos. 1/4, 207–17, 2 graphs.

This is practically a repetition of the previous paper the results being those obtained in another non-endemic area of Rumania where only scanty sporadic cases of malaria occur (Sibiu, Transylvania).

The findings confirm previous experience that patients from non-endemic areas have less immunity to malaria than those from endemic areas.

H. E. Shortt

Young, M. D., Eyles, D. E. & Burgess, R. W. **Studies on Imported Malarias. 10. An Evaluation of the Foreign Malarias introduced into the United States by Returning Troops.** *J. National Malaria Soc.* 1948, Sept., v. 7, No. 3, 171–85. [38 refs.]

Nine reports on studies in the United States of returned military personnel with malaria acquired overseas have previously been published, and summarized in this *Bulletin* [1946, v. 43, 5, 1002 ; 1947, v. 44, 275, 492 ; 1948, v. 45, 236, 298, 859, 1052, 1053]. This tenth report summarizes the findings of the entire programme of studies. The observations were carried out in ten Army and Navy hospitals, and foreign strains of malaria were used in the treatment of neurosyphilis in eight other institutions. About 1,000 members of the Forces with relapsing malaria were examined ; another 1,000 patients or volunteers were infected with one or other of the malaria strains isolated. There was no infection with *P. malariae* and only 8 cases of *P. falciparum* infection. One of the latter from Guadalcanal infected *A. m. freeborni*, and another from Africa infected *A. quadrimaculatus*. Most of the studies concerned *P. vivax*.

No consistent morphological differences could be detected between imported and indigenous strains of *P. vivax*. In two different *P. vivax* infections from New Guinea, forms resembling *P. ovale* were found on a few occasions but their occurrence was transient ; they were probably abnormal forms of *P. vivax*.

There was but little heterologous immunity between *P. vivax* infections from the South Pacific, China-Burma-India theatres and from the United States. One infection from New Guinea showed little immunity to another strain from the same area. Prepatent and incubation periods were shorter in infections with Mediterranean than with Pacific strains.

American Negroes are resistant to *P. vivax* of both Pacific and Mediterranean origin. In one study, 31 per cent. of Negroes bitten by infected mosquitoes became infected as compared to 95 per cent. white patients.

When the fever first reached 100°F. the number of parasites of Pacific strains averaged only 21 per cmm. ; the average number of parasites of Mediterranean strains was 45. Peak parasitaemias, averaging about 14,000 per cmm., were usually attained in the second week and were generally higher in Pacific than in Mediterranean infections. Maximum temperatures (average 105°F.) tended to occur several days earlier than maximum parasitaemias. In tertian fevers the periodicity, average time between fever peaks, was 44·4 hours for four Pacific strains and 45·1 hours for one Mediterranean strain ; none had a 48-hour periodicity.

Two hundred patients with delayed primary attacks were studied, mostly from New Guinea. The delayed primary attack occurred 49·1 days (average) after cessation of suppressive mepacrine. The parasite-fever thresholds in 65 patients were 730 parasites per cmm. in delayed primary attacks and 1,980 in subsequent relapses, both much higher than in induced attacks with similar strains.

The foreign malarias responded well to treatment ; of the commonly-used drugs, chloroquine was the most effective, quinacrine next, and then quinine, the poorest.

A smaller proportion of Mediterranean malarias relapse than of those from the Pacific. With a Pacific strain (Chesson) it was found that the greater the sporozoite inoculum, the shorter the prepatent period, the greater the relapse rate and the shorter the interval between relapses.

The comparative susceptibility to foreign *P. vivax* malarias of five anophelines, (the infective index of the most susceptible being expressed as 100) was found to be : *A. m. freeborni* 100 ; *A. punctipennis* 86 ; *A. quadrimaculatus* 84 ; *A. p. pseudopunctipennis* 41 ; *A. albimanus* 2. Some foreign strains have been maintained unimpaired through many man-mosquito transfers : they have very readily adapted themselves to new mosquito hosts.

Compared with indigenous strains, foreign malarias relapse more promptly after treatment of primary attack and produce a greater number of relapses. Parasitic relapses are not always accompanied by symptoms ; the total time of asymptomatic parasitaemia is considerably greater than the time of symptomatic parasitaemia. In general the number of gametocytes was found to be a fairly constant proportion of total parasites present. The patient with asymptomatic parasitaemia is the one most likely to spread the disease in the conditions prevailing in the United States.

In 1945 there may have been in the United States as many cases of foreign *P. vivax* malaria as there were cases of indigenous strains (estimated at about 20,000). *Norman White*

Hoehne, K. Über Rezidivneigung und Konstitution bei Malaria. Ein Beitrag zur Frage der Abhängigkeit des Infektionsverlaufes vom Konstitutionstyp. [**Constitution and the Tendency to Relapse in Malaria. A Contribution on the connexion between the Course of Infection and the Bodily Formation.**] *Deut. med. Woch.* 1948, Nov. 5, v. 73, Nos. 41/42, 530–31, 1 fig. [10 refs.]

Sanders, J. P. & Sanders, J. C. **Intravenous Quinine in Post-War Malaria.** *Med. Times.* New York, 1948, Nov., v. 76, No. 11, 465–9.

A study of 271 cases of chronic malaria, 259 being civilians and 12 ex-servicemen. No attempt was made to identify the type of parasite although it is considered that the majority were of the benign tertian or tertian [*sic*] variety. Diagnosis was made largely from the history, symptoms, and physical igns, parasites [variety not stated] being found in only 72 patients in spite of outine examination of thick and thin films repeated many times in some

instances. Most of the patients had a leucopenia and high count of small lymphocytes, while the spleen was almost always enlarged and tender.

Intravenous injections of 5 to 15 grains of quinine dihydrochloride in 1,000 cc. of 5 to 10 per cent. glucose were given, the usual dose of quinine being 10 grains. Injections were usually repeated after 2 or 3 days, although occasionally they were given daily, the number and frequency being determined by the patient's reaction and condition.

Among the 259 civilian cases, a history of previous attacks was given in 64 per cent. Headache was the most prominent complaint although, as might be expected, symptoms of almost every known disease were complained of, and many cases of resistant cough for which the patients had been X-rayed for tuberculosis, cleared up under treatment.

One patient had 12 injections and 3 patients had more than this number. The highest age group was over 50 (71 patients) while 22 were under 20. "Coloured people" numbered 34. Of the 12 ex-servicemen most had taken atebrin [mepacrine] while abroad, and received other medication at some time.

The authors claim for this method of treatment :—

(1) Complete relief of all symptoms in practically every case.
(2) Toleration in all age groups, especially the aged.
(3) A general tonic effect, possibly due to the glucose.
(4) Decrease in toxic effects, while many of the side effects of quinine by mouth are avoided.
(5) Safety in allergic subjects, although a few patients had to discontinue treatment on this account. Any reactions noted were not usually serious. Only 22 per cent. of relapses were reported within two years.

[As the authors point out, it was impossible to exclude reinfection in Louisiana and it must be remembered that 176 cases had other treatment by mouth, *e.g.* quinine, quinidine, totaquina, mepacrine, aralen. It is rather difficult to assess the value of this method *per se.*] *C. F. Shelton*

MARSHALL, P. B. & ROGERS, E. W. **The Determination of Quinine Degradation Product in Blood, and its Absorption in the Chick.** *Biochem. J.* 1948, v. 43, No. 3, 414–16, 1 fig.

"(1) A method for the quantitative determination of quinine degradation product (QDP), sensitive to 5 μg., is described.

"(2) The red-cell concentration of QDP in chicks during 7 hr. following oral doses is approximately the same as that of an equal dose of quinine, indicating that the previously observed higher antimalarial activity of quinine is due to higher specific activity on the parasite, and not to superior absorption in the host."

CIUCA, M., SOFLETE, A., CONSTANTINESCO, P. & TERITEANU, N. **Preliminary Note on the Therapy of Malaria with Paludrine in Experimental Infection by Inoculation of Infected Blood.** *Bull. World Health Organization.* 1948, v. 1, No. 2, 301–7.

A Rumanian strain of *P. vivax* that had gone through 279 passages was used. Forty patients were inoculated. Of these 8 received one dose of 100 mgm. paludrine, 7 between the 4th and 8th days of fever, and one after he had had paroxysms for a fortnight. In 7 cases, fever disappeared within 24 hours of the administration of paludrine ; in the other temperature was normal 3 days after the drug was given. In 2 cases, parasites were absent from thick drops on the third day, in 4 on the 4th, and in 2 on the 5th day. Twenty-four

patients were treated with 200 mgm. of paludrine for 7 days ; the fever ceased after an average period of 1·65 days and parasites disappeared after an average of 3·65 days. Similar results were obtained in eight patients treated with 300 mgm. paludrine a day for 7 days. A single dose of 100 mgm. is amply sufficient to avert the attack.

Nine patients were inoculated with an African strain of *P. malariae* in its 137th passage. They each received 200 mgm. paludrine a day for 7 days, the treatment starting from the 4th to the 10th day of fever in 4 cases, from the 10th to the 15th in 4 cases, and on the 24th day of fever in one case. On an average, the fever disappeared in 1·88 days and the parasites after 8·8 days (3 to 14). In only 3 patients did the parasites disappear during the course of the 7 days' treatment. Results similar to these were obtained in 4 patients treated with 600 mgm. paludrine a day for 7 days, and in 12 others treated with 600 mgm. a day for ten days. *P. malariae* shows a degree of resistance to paludrine comparable to that previously observed to other schizonticidal drugs. *Norman White*

Chaudhuri, R. N. & Chakravarti, H. **Intravenous " Paludrine " (Proguanil).** *Brit. Med. J.* 1949, Jan. 15, 91–3, 1 fig.

Eleven patients suffering from malaria in Calcutta were treated with intravenous injections of paludrine acetate (soluble proguanil). Eight had *P. falciparum*, 2 *P. vivax* and one mixed infections. Most of the patients had serious cerebral or gastro-intestinal complications that rendered their cases unsuitable for medication by mouth. Details are given of each case. At first the dose was 100 to 200 mgm. repeated two or three times at intervals of four-hours. Later it was a single dose of 300 or 400 mgm. The total amount of paludrine per case injected ranged from 200 to 600 mgm. With the higher doses the blood became clear of parasites in from 24 to 48 hours and the temperature fell to normal in from 32 to 72 hours. One patient in a moribund state died. Another with typical cerebral malaria remained unconscious for several days, developed signs and symptoms of encephalitis, but ultimately recovered. The injections were well tolerated ; one patient, however, had transient phlebitis of the injected vein. *Norman White*

Covell, G., Nicol, W. D., Shute, P. G. & Maryon, M. **" Paludrine " (Proguanil) in Prophylaxis and Treatment of Malarial Infections caused by a West African Strain of** *P. falciparum*. *Brit. Med. J.* 1949, Jan. 15, 88–91.

The authors refer to the very divergent accounts of the efficacy of paludrine in the treatment and prophylaxis of malaria that have emanated from different parts of Africa and elsewhere. To clear up some of the points at issue they undertook a series of prophylactic and therapeutic trials at Horton Hospital, Epsom, using a strain of *P. falciparum* from Lagos, Nigeria. Laboratory-bred *A. stephensi* were used for transmission. Twenty-seven patients were used in the prophylactic tests ; they were each infected once a week over a period of six weeks. Drug administration was started three days before the first infection and continued until the sixth day after the last infection. The dosages of paludrine used were : 100 mgm. daily ; 50 mgm. daily ; 100 mgm. twice weekly; 300 mgm. once weekly—five patients in each group, together with 7 controls (2 on quinine and 5 on no drug). Paludrine was found to act as a true causal prophylactic against this strain of *P. falciparum*. The prophylactic dose recommended for non-immune adults exposed to malaria infection in West Africa is 100 mgm. daily.

Twenty-five other patients were used in the therapeutic tests, the schedules and results are shown in tables ; paludrine controlled the clinical attacks in

these patients but its action, both as regards the persistence of fever and of parasites in the peripheral blood, was somewhat slower than that of mepacrine or quinine. Paludrine unaided failed to effect radical cure of infections with this strain : this was in marked contrast with the results of FAIRLEY *et al.* with New Guinea strains [this *Bulletin*, 1947, v. 44, 282]. Radical cure was apparently obtained with 300 mgm. paludrine twice daily for 10 days *plus* 900 mgm. of mepacrine given in 3 doses on the first day of treatment (6 cases) [shown in the table as 5] ; with 300 mgm. paludrine twice daily for 10 days *plus* 30 grains (2 gm.) quinine hydrochloride given in 3 doses on the first day of treatment (5 cases) ; and with 10 grains (650 mgm.) of quinine hydrochloride twice daily for 10 days (5 cases).

After a course of 300 mgm. paludrine twice daily for 10 days gametocytes were non-infective to mosquitoes.

A course of paludrine, 300 mgm. twice daily for 10 days, together with 900 mgm. mepacrine in 3 doses on the first day, shortened the duration of clinical symptoms by about 24 hours. Such a course, followed by a maintenance course of 100 mgm. paludrine a day for the following six weeks, should secure rapid termination of the clinical attack, a high radical cure rate and sterilization of gametocytes with a minimum risk of toxic effects. *Norman White*

BURN, J. H. & VANE, J. R. **The Inhibitory Action of Paludrine on the Secretion of Gastric Juice.** *Brit. J. Pharmacol. & Chemotherapy.* 1948, Dec., v. 3, No. 4, 346–9, 2 figs. [12 refs.]

The increased secretion of gastric juice which occurs in patients with peptic ulcer can also be produced by histamine. During or between periods of intravenous infusion of the latter substance to anaesthetized cats, the inhibitory effect of paludrine and related substances on the secretory flow was determined and provided a severe test of such action. The drugs for test were administered in a single intravenous dose or by infusion. Sometimes there was a transitory rise in secretion immediately after administration. Paludrine reduced secretion both as regards volume and amount of free acid present. The only other substance with comparable activity was that in which a methyl group replaced the isopropyl group of paludrine. Gastro-intestinal symptoms in man and anorexia in dogs, which may arise from administration of paludrine, are probably related to the present findings. *J. D. Fulton*

VANE, J. R., WALKER, J. M. & PARRY, C. B. W. **The Effect of Paludrine on Gastric Secretion in Man.** *Brit. J. Pharmacol. & Chemotherapy.* 1948, Dec., v. 3, No. 4, 350–51.

" 1. The effect of paludrine on gastric acidity has been investigated by carrying out test meals on 9 subjects.

" 2. A significant reduction in acidity occurred when 0·9–1·0 g. paludrine was given by mouth 2 hours before the test meal.

DOLL, R. & SCHNEIDER, R. **The Effect of Paludrine on Human Gastric Secretion.** *Brit. J. Pharmacol. & Chemotherap.* 1948, Dec., v. 3, No. 4, 352–3.

" 1·0 g. paludrine hydrochloride given 2 hours before the start of a gruel test meal produced a significant depression of more than 33 per cent. in the concentration of free acid during the first 1½ hours of the meal. No consistent effect was observed with doses of up to 400 mg. paludrine acetate given intravenously on the gastric secretion in response to histamine."

i. British Med. J. 1949, Jan. 15, 106–7. **Second Thoughts on Proguanil.** [16 refs.]

ii. Covell, G. **Second Thoughts on Proguanil.** [Correspondence.] *Brit. Med. J.* 1949, Jan. 29, 192.

i. A leading article in the *British Medical Journal* deals with the fact that many new pharmaceuticals in the past quarter of a century have failed to live up to the high reputation that early therapeutic trials had engendered. Paludrine, now known as proguanil, is taken as an example. Reference is made to many discordant results, with numerous strains of malaria from different parts of the world, which have recently been published. On the debit side it is stated that complaints have been made of loss of appetite, reduction of weight, and lack of energy from some of those who have taken proguanil for considerable periods. A comparison is made of the effects of mepacrine and proguanil, respectively, in the treatment of falciparum malaria in West Africa. "It is thus doubtful whether the ideal drug either for the prophylaxis or radical cure of malignant tertian malaria has yet been discovered".

ii. Covell challenges the assertion that proguanil in doses generally used for prophylaxis or treatment has any adverse effect on the digestive system. One of the outstanding advantages of the drug is due to the extremely wide margin between its effective and toxic dosage; it is particularly suitable for prophylaxis and treatment among indigenous populations of malarious countries. A single-dose treatment of 300 mgm. for the clinical attack, and a single weekly dose of 300 mgm. for prophylaxis have been widely used in India, Malaya and parts of Africa. Large numbers of British troops have been taking 100 mgm. of proguanil a day over extended periods, and no reports suggesting an adverse effect on appetite have yet been forthcoming. Covell examines critically the results of experiments by Schmidt *et al.* on animals [see below] and of those workers primarily concerned with a drug which might inhibit the secretion of gastric juice in the treatment of chronic peptic ulcer, [above] in support of his arguments relating to the effects of proguanil in the dosages used in man for the prophylaxis of malaria [see Covell *et al.*, above]. "It would be most unfortunate if an impression were to be created, on such slender evidence, that the prophylactic use of proguanil is likely to have an adverse effect on the nutrition of any population to whom it is administered."

Norman White

Schmidt, L. H., Hughes, Hettie B. & Smith, C. C. **On the Pharmacology of N_1-Para-Chlorophenyl-N_5-Isopropylbiguanide (Paludrine).** *J. Pharm. & Exper. Therap.* 1947, July, v. 90, No. 3, 233–53, 1 fig. [17 refs.]

Spinks & co-workers have reported on the estimation, excretion and tissue distribution of paludrine in laboratory animals [this *Bulletin*, 1946, v. 43, 400, 707; 1947, v. 44, 35]. The present authors have used rats, mice, dogs and monkeys for a pharmacological and physiological study of the same substance. In the mouse, continued oral treatment in sublethal doses did not affect growth or general well-being; in the rat effects were slight. Intramuscular dosage was less well tolerated. In animals generally the chief effect of the drug during chronic toxicity tests with a certain dosage was impairment of appetite with consequent effect on growth. No pathological lesions were noted in the tissues of the rat or mouse. Experiments on dogs and monkeys were conducted in similar fashion; the drug being administered by stomach tube. The chief toxic symptoms in the dog were salivation, bilious vomiting and loss of appetite. In fatal cases there was marked haemo-concentration with increase in haemoglobin and red cell count, whereas white cell counts did not differ significantly from

normal. Intoxicated animals exhibited bradycardia, but again no gross changes were present in the organs. Recovery from the effects of paludrine was rapid when the drug was discontinued, in marked contrast to the results obtained with quinacrine [mepacrine] or chloroquine. For estimation of paludrine the method noted above was used when absorption and tissue distribution was being investigated. When given by stomach tube absorption of the drug was complete but not rapid. Plasma levels reached a peak value in 2 hours and declined to zero within 24 hours. The levels attained were generally in proportion to dosage, but differences were apparent in different animal species as well as in individuals of the same species. The amounts present in different tissues during chronic toxicity tests varied widely in different organs, but there was no tendency for accumulation except perhaps in the liver at the higher doses. In the rat, excretion was mainly in the faeces and to a smaller extent in the urine. Some drug was secreted into the bowel, partly in bile. The results obtained from estimation of the amount of paludrine in the tissues and excretions suggested that approximately half the drug administered was being metabolized. Comparison of the toxaemias produced by paludrine, quinacrine [mepacrine] and chloroquine showed that the first named possessed advantages in that the adverse effects were confined to the gastro-intestinal tracts, were readily detected and easily reversed. The drug, moreover, did not tend to accumulate like the two latter drugs. *J. D. Fulton*

CANET, J. Essais de traitement curatif du paludisme aigu par un nouveau dérivé synthétique : la nivaquine C. [**Treatment of Acute Malaria with a New Synthetic Derivative, Nivaquine C.**] *Bull. Soc. Path. Exot.* 1948, v. 41, Nos. 9/10, 584–8.

The author reports the treatment of 120 patients in Cochin China suffering from acute malaria with Nivaquine C. Of these patients 101 were agricultural workers, originally from Tonking, *P. falciparum* 91, *P. vivax* 10 ; 14 were Annamite children, aged 2 to 13, *P. falciparum* 10, *P. vivax* 4 ; 5 European adults, *P. falciparum* 1, *P. vivax* 4. All had been long settled on a rubber plantation in a hyperendemic malarious region. All had suffered from repeated attacks of malaria and all had large spleens. There was no case of primary infection. All had typical acute attacks of malaria ; pernicious attacks and cases of malarial cachexia were excluded from the inquiry.

All patients received 0·3 gm. of Nivaquine C a day (adult dose) until two successive blood examinations both failed to reveal schizonts : thick drops and smears were examined night and morning. In *P. falciparum* infections, 62 per cent. of patients were free from fever on the second day ; 93 per cent. were free from fever on the third evening. In *P. vivax* infections fever disappeared somewhat more rapidly. *P. falciparum* schizonts disappeared in 24 per cent. of cases on the third day ; in 52 per cent. on the fourth day, and in 20 per cent. on the fifth day. *P. vivax* schizonts were somewhat more persistent, but by the fifth day 95 per cent. of patients were parasite-free.

Nivaquine C appears to be completely ineffective against the gametocytes of *P. falciparum*.

The author concludes that the antimalarial action of Nivaquine C is identical with that of quinacrine to which it is preferable inasmuch as its toxicity is very low and it does not discolour the skin. The adult dose of 0·3 gm. a day is sufficient for the treatment of a typical acute attack : doses as high as 1·0 gm. a day are well tolerated. For grave forms of malaria and pernicious attacks, the author still employs intravenous quinine medication. *Norman White*

CURD, F. H. S., LANDQUIST, J. K. & ROSE, F. L. **Synthetic Antimalarials. Part XXXI. 2-p-Chloroanilino-4-β-Diethylaminoethylamino-quinazolines containing various Substituents in the Quinazoline Nucleus.** *J. Chem. Soc.* 1948, Nov., 1759–66.

CURD, F. H. S., HOGGARTH, E., LANDQUIST, J. K. & ROSE, F. L. **Synthetic Antimalarials. Part XXXII. Some 4-Arylamino- and 4-Arylthio-2-aminoalkylaminoquinazolines, and 2-Arylthio-4-amino-alkylaminoquinazolines.** *J. Chem. Soc.* 1948, Nov., 1766–73.

HEYMANN, H. & FIESER, L. F. **Naphthoquinone Antimalarials. XXI. Antisuccinate Oxidase Activity.** *J. Biol. Chem.* 1948, Dec., v. 176, No. 3, 1359–62.

FIESER, L. F. & HEYMANN, H. **Naphthoquinone Antimalarials. XXII. Relative Antirespiratory Activities** (*Plasmodium lophurae*). *J. Biol. Chem.* 1948, Dec., v. 176, No. 3, 1363–70, 1 fig.

CIUCA, M., BALIFF, L. & CHELARESCO, M., with the co-operation of A. TIMISESCO, F. VASILIU-MUNTEANU & M. V. TROFIN. **Trials of Causal Prophylaxis of Malaria with Paludrine.** *Bull. World Health Organization.* 1948, v. 1, No. 2, 297–300, 3 figs.

An old strain of *P. falciparum* used for malaria therapy in Rumania was used in these experiments.

Of 5 subjects inoculated with a single dose of sporozoites and given 100 mgm. paludrine on the day of inoculation and on the three following days, 2 developed infection after incubation periods of 29 and 35 days; one developed only parasitaemia; the remaining two showed neither fever nor parasites during 57 and 66 days observation, respectively. Of 3 untreated controls one developed a slight infection after 11 days incubation, one an ordinary infection, and the third showed only parasitaemia after a long incubation period.

In a second series, 100 mgm. paludrine was continued until the 6th day of the incubation period. Of four patients inoculated with at least 280,000 sporozoites and treated as above, one developed infection after 34 days, and a second parasitaemia after 35 days incubation. The other two developed neither fever nor parasitaemia during observation periods of 23 and 156 days. The dosage in both these series was insufficient to achieve causal prophylaxis.

In a third series, five subjects were inoculated with sporozoites repeated over a period of 4 weeks. They were given 100 mgm. paludrine once weekly during this period and two further weeks. They developed fever and parasitaemia 7, 18, 6, 6 and 9 days after the final dose of paludrine. There was no causal prophylaxis.

In a fourth series, 5 subjects were inoculated with sporozoites twice a week over a period of 4 weeks. Paludrine 300 mgm. was given once a week during inoculations and continued for a further two weeks. None developed fever and there was no parasitaemia during at least 23 days after final inoculation. Four untreated controls developed the disease after incubation periods of from 12 to 15 days. *Norman White*

DAVIDSON, G. **"Gammexane" and Mosquito Control in the Belgian Congo.** *Brit. Med. J.* 1949, Jan. 15, 101–2.

For the purposes of mosquito control water-dispersible powders containing gammexane have been sprayed on the internal surfaces of African houses in a palm-oil plantation and neighbouring villages in Yaligimba, Belgian Congo, aiming at a concentration of 10 mgm. of gammexane per square foot.

Eclipse " Warley " pneumatic sprayers have applied 5 pints of spray per 1,000 square feet of surface.

Results so far indicate a very marked reduction in the number of anopheline mosquitoes caught by four methods :—

(*a*) Pyrethrum in kerosene spray and white sheets on the floor.

(*b*) Window-traps to catch mosquitoes leaving each morning.

(*c*) Mosquito net traps attached to a bed, which show numbers of mosquitoes entering at night to bite occupants of one bed.

(*d*) The personal calico nets of the inhabitants, acting as traps because of bad state of repair or incomplete closure. This result is expressed as a percentage of nets containing mosquitoes.

The unreliability of estimating the persistence of the insecticide by determining mosquito densities by the flit-catching method alone has been clearly demonstrated. Fifteen or sixteen weeks appears to be the period of maximum effect of the insecticide.

The principal anopheline is *A. moucheti* which breeds at the edges of the large rivers in this tropical forest type of country ; a few *A. gambiae* and *A. paludis* occur. Salivary gland dissections (tabulated) indicate an absence of infected mosquitoes in the treated villages as compared to 0·40 per cent. *A. moucheti* and 4·17 per cent. *A. gambiae* infections in untreated villages.

For malaria control purposes in this particular area it is thought that an initial spraying of the whole area three times during the first year can be reduced to twice a year.

[This is a preliminary report and will be followed by a more detailed account.]

R. Ford Tredre

HEISCH, R. B. & WILSON, D.A.O. **Preliminary Trial with 5 lb. D.D.T. Smoke Generators against Mosquitoes.** *East African Med. J.* 1948, Oct., v. 25, No. 10, 400–406.

An endeavour to assess under field conditions the value of DDT smoke as a means of killing adult mosquitoes and larvae at their natural breeding places yielded inconclusive or negative results.

The methods of assessment were by the exposure of adult mosquitoes in cages, the exposure of larvae in bowls and the counting of larvae in the swamp ; the numbers of survivors were high and, under the conditions of the experiment, the mortality may or may not have been due to DDT.

The authors concluded that the 5 lb. DDT smoke generator is unlikely to be of any value in malaria control in East Africa.

[The result of the analysis of swamp vegetation for DDT deposit is not included.]

R. Ford Tredre

DA COSTA, A. M. & BASSÈRES, M. S. Ação do DDT sobre o *A. darlingi*, *A. albitarsis* e outros Culicideos. [**Action of DDT on** *Anopheles darlingi* *A. albitarsis* **and other Mosquitoes.**] *Rev. Serviço Especial de Saúde Pública.* Rio de Janeiro. 1948, May, v. 1, No. 4, 997–1008, 1 graph. English summary.

These experiments were made at Alfredo Maia, Brazil during 1946 and 1947. Weekly collections of anophelines from houses during the previous two years had shown that the number varied between 6·6 to 7·5 per standard collection.

Ten of the houses were then sprayed with DDT in water at 3·5 gm. DDT per square metre ; ten others at 2·5 gm. DDT per square metre ; similar groups of houses were treated with 2½ per cent. DDT in kerosene at the same rates ; seven houses were treated with a pyrethrum insecticide at 2 gm. pyrethrum per square metre and ten houses were untreated.

Collections of mosquitoes were made from all houses for twenty-seven weeks after treatment. These captures were separated into *Anopheles darlingi*, *A. albitarsis* and "other mosquitoes". The weekly figures for living and dead mosquitoes taken from each group of houses are given in tables.

The total numbers of mosquitoes found dead in each experimental group are given as :—DDT/water at 3·5 gm., 197 (93·8 per cent.) ; DDT/water at 2·5 gm., 72 (93·5 per cent.) ; DDT/kerosene at 3·5 gm., 86 (80·0 per cent.) ; DDT/kerosene at 2·5 gm., 100 (73·0 per cent.) ; pyrethrum, 30 (27·3 per cent.) and in the control group of houses, 9 (2·6 per cent.). The two concentrations of DDT in water were equally effective. During the last few weeks of the experiment, the number of mosquitoes captured alive in houses treated with DDT in kerosene formed 85·4 per cent. of the total number of living mosquitoes found in DDT-treated houses ; the authors therefore consider that DDT in water suspension has better lasting qualities than DDT dissolved in kerosene.

H. S. Leeson

Deane, L. M., Freire, E. P. S., Tabosa, W. & Ledo, J. A aplicação domiciliar de DDT no contrôle da malária êm localidades da Amazônia. [**House Spraying with DDT in Malaria Control in Amazonia.**] *Rev. Serviço Especial de Saúde Pública*. Rio de Janeiro. 1948, May, v. 1, No. 4, 1121–61, 9 figs. English summary.

An account is given of a large-scale programme of residual spraying with 5 per cent. DDT in kerosene in buildings in the Amazon region of Brazil, having as its ultimate aim the prevention of malaria by the destruction of its vector *Anopheles darlingi*.

The results obtained in 1945 in the small town of Breves were so successful that the treatment was extended to other areas, and by September, 1947, a total of 27 areas, with a population of approximately 33,000, were being treated. At first, the spraying of the houses was done every two months but later a four-month interval was established. Some localities were regarded as experimental areas, but in others the treatment was applied to all buildings (7,303).

The inner surfaces of the walls were sprayed to a height of 3 metres at an average concentration of 2·113 gm. DDT per square metre.

A survey in Breves before spraying started, showed that 22 per cent. of the blood slides were positive for plasmodia and gave a spleen rate of 45 per cent. In May, 1946, after one year of bi-monthly spraying, these rates were 1·5 and 16·8 per cent. respectively ; a year later they were 0·3 and 8·3 per cent., respectively. Three months after spraying started, no *A. darlingi* could be found in the houses, and after the sixth month only sporadic cases of malaria occurred. Among children born during this campaign there was no malaria.

In other towns, surveys made before and after DDT treatment, showed that the parasite rate fell from 9·9 to 3·1 per cent. and the spleen index from 24·6 to 13·7 per cent. The number of malaria cases was only 43·3 per cent. of the number recorded before treatment during a corresponding period ; but in untreated localities this figure was 90·9 per cent.

In Manaus, Amapa, Macapa and Mazagão, *A. darlingi* had either become very rare or had completely disappeared from houses.

Methods are described and costs are given, as also are the complete figures for each locality, maps of the areas and samples of the record forms. Photographs show details of the type of equipment used.

H. S. Leeson

Penido, H. M., de Sousa, E. F., Pinto, D. B. & Bezerra, F., Jr. Expurgo domiciliar com DDT considerações de ordem economica. [**House Spraying with DDT ; Economic Considerations.**] *Rev. Serviço Especial de Saúde Pública.* Rio de Janeiro. 1948, May, v. 1, No. 4, 1163–70. English summary (10 lines). Also in *Rev. Hig. e Saúde Pública.* 1947, Oct.–Dec., v. 5, No. 3, 78–84.

The authors discuss the cost of the DDT house-spraying campaign in the River Doce Valley after experience of four cycles of spraying [see also this *Bulletin*, 1948, v. 45, 391, 408]. In most of the area houses are very sparsely scattered and transportation expenses have been in consequence very high. They think that very considerable economies might be achieved by decentralization. Each county should be made responsible for the upkeep of trained staff and equipment and for the prosecution of the work, importing DDT direct from the producing country.

Norman White

Alvarado, C. A. & Coll, H. A. Programa para la erradicación del paludismo en la República Argentina. [**Programme for the Eradication of Malaria in Argentina.**] *Bol. Oficina Sanitaria Panamericana.* 1948, July, v. 27, No. 7, 585–602. English summary.

This paper describes an ambitious programme whereby it is hoped to eradicate malaria from Argentina by the use of DDT. Malaria is endemic over an area of 120,000 square kilometres in the north-east of the country in the plains and valleys along the foothills of the Andes, extending from Bolivia to 32°S. Here the vector is *A. pseudopunctipennis*. The transmission season begins at the end of October in the north of the area, but not till the end of the year in the south. There is no transmission in the cooler months, June to October.

Occasional outbreaks of malaria also occur in the extreme north-east of Argentina, in districts bordering Paraguay and Brazil. Here the vectors are probably *A. albitarsis*, an indigenous species, and *A. darlingi*, which comes from across the frontier.

The population of the endemic area approximates one million, nearly a third of whom suffer from malaria each year.

Experiments with DDT were started at the end of 1946 and gave promising results. An attempt is now to be made to deal with the whole of the infected area. The headquarters of the organization is in Tucuman. The first year's work is designed to give protection to 40 per cent. of the affected population ; this will be extended to 80 per cent. in the second year. Interior walls of dwellings will be sprayed with a 5 per cent. solution or suspension of DDT, 2 gm. per square metre. The first spraying will be done at least a month before the vector becomes active and will be repeated at intervals of three months till the end of the transmission season.

Norman White

Ferreira, M. O. Combate específico ao vetor de malária, em zona de transmissão por anofelinos do sub-gênero " Kerteszia ". [**Control of Malaria Vectors in an Area where Transmission is by *Kerteszia*.**] Reprinted from *Malariologia e Doenças Tropicais.* Rio de Janeiro. 1948, July–Sept., v. 1, No. 1, 8 pp., 1 fig.

The English summary appended to the paper is as follows :—

" The malaria control on the coast of the State of Santa Catarina (south of Brazil), where the vectors are anophelines of the subgenus *Kerteszia* (bromeliad-breeding anophelines), can be done by three methods : (1) the hand removal

of bromeliads: (2) the spray killing of bromeliads, applying herbicides (3) forest control (cutting out the trees around towns.)

"The first method has been used since 1944 and gave some satisfactory epidemiological results, but it shall not solve the problem. The second one, the spray killing of bromeliads has little indication on account of the topography of the region and the vegetation type: the forests are very high and on hillsides.

"The author thinks that forest control is the indicated method to the solution of the bromeliad-malaria problem of the State of Santa Catarina."

RIGDON, R. H. **Effect of Blood and Oxygen on *Plasmodium knowlesi* Infection in Monkeys.** *Amer. J. Hyg.* 1948, Sept., v. 48, No. 2, 147–57, 7 figs. [11 refs.]

Studies on the pathology of ducks infected with *Plasmodium lophurae* and monkeys infected with *P. knowlesi* have shown that lesions similar to those occurring in shock are found, and it is believed that these are due to anoxia. The experiments described in this paper were the application of results obtained with *P. lophurae* and ducks to monkeys (*M. mulatta*) infected with *P. knowlesi*. Monkeys were infected by blood inoculation and at various stages of the infection were subjected to the following lines of treatment:—

(*a*) Placed in an oxygen chamber with an oxygen concentration of 40–60 per cent.
(*b*) As in (*a*) but given small doses of quinine.
(*c*) Transfused with type O human blood from syphilitic donors.
(*d*) As in (*c*) but with the monkey placed in the oxygen chamber.
(*e*) Transfused with blood and given quinine.
(*f*) Treated with oxygen, blood and quinine.

The numbers of monkeys used in these five series were 5, 2, 2, 3, 1 and 6, respectively. These numbers are much too small for any conclusions to be drawn from the experiments and they certainly do not, in themselves, justify all the statements made in the author's summary, in which the use of oxygen and blood transfusions is suggested as supportive therapy in acute malarial infections in man. Considering the fact that in the whole series there were very few survivors, whereas the use of adequate doses of quinine alone would probably have saved the majority, the elaborate treatments used, would appear unnecessary. *H. E. Shortt*

DEARBORN, E. H. **A Comparison of One Dose per Day with Six Doses per Day of Quinine in the Suppression of Lophurae Malaria in the Duck.** *J. Pharm. & Exper. Therap.* 1948, Oct., v. 94, No. 2, 178–81.

MARSHALL & DEARBORN have shown previously [this *Bulletin*, 1947, v. 44, 292] that the minimal effective dose of quinine administered once per day by stomach tube to chicks infected with *P. lophurae* was smaller than when it was given by the drug-diet method (corresponding to continuous dosage). By the latter method, however, the drug intake could not be accurately determined and treatment was begun previous to inoculation, before the infection was established. To avoid criticisms in this respect, treatment in this investigation was not started till 24 hours after intravenous inoculation with $150 \cdot 10^6$ parasitized erythrocytes. Groups of ducks were treated with a daily dose of quinine by stomach tube and others at intervals of 4 hours over the same period of 4 days. The single doses given were 4, 8, 16 and 32 mgm. of base per kilo, and the repeated doses 2, 4, 8 and 16 mgm. per kilo. It was found that the amount of quinine required to suppress the infection when given as a single dose was about one-third of that necessary when the doses were given every

4 hours. By estimation of quinine in plasma the authors [this *Bulletin*, 1946, v. 43, 404] have shown that, in contrast to the known facts about sulphonamide drugs, the maintenance of a certain concentration in blood was not necessary for the suppression of *P. lophurae* infections in ducks. Studies by other authors have indicated that in the case of certain infections the same is true of penicillin and streptomycin. The results are of theoretical and practical interest.

J. D. Fulton

BACIGALUPO, J. Etapa invisible del *Plasmodium gallinaceum* Brumpt, 1935. [**An Invisible Stage of** *Plasmodium gallinaceum*.] *Semana Méd.* 1948, Dec. 2, v. 55, No. 49, 1151–4.

The author, in 1943, obtained a strain of *P. gallinaceum* and has kept it going. Examination of the plasma of infected birds did not reveal any parasites, nevertheless injection of it did, in some cases, set up infection. The question then arose as to whether the infective material was or was not capable of passing through a filter—the disk sterilizing filter of the Filter Corporation, New York.

The plasma diluted with Ringer's solution and injected intramuscularly caused the signs of infection to appear in 8–18 days, whereas when injected similarly after dilution and filtration infection was observed in 25–30 days. Intracerebral inoculation of blood containing parasites might give rise to symptoms as early as 15 hours after, or as late as 4 days.

The author discusses the possible implications of these results.

H. Harold Scott

LEWERT, R. M. **Exoerythrocytic Infection by** *Plasmodium gallinaceum* **in Blood-infected, Quinine-treated Chicks; with special reference to the Central Nervous System.** *Amer. J. Hyg.* 1948, Sept., v. 48, No. 2, 158–70, 6 coloured figs. on 1 pl. [13 refs.]

An account is given of the sites of invasion in the tissues of the chick, treated with quinine, by the exoerythrocytic forms of *Plasmodium gallinaceum* with special reference to the forms seen in the brain. The infections were produced by blood inoculation and the results of the experiments may be summarized shortly :—

(*a*) All parts of the brain were invaded by exoerythrocytic parasites.

(*b*) Although the intensity of the infections varied in individuals, there was a general agreement with regard to the parts of the brain most highly parasitized. The difference in parasite density appeared to be directly related to the richness of the capillary circulation, the parasitism being greatest where the capillaries were most numerous and especially where they were relatively unbranched.

(*c*) The quinine therapy suppressed the primary parasitaemia, but when the exoerythrocytic density became great, young ring forms of the erythrocytic series, unaccompanied by older forms, were able to invade the erythrocytes.

(*d*) Blocking of the capillaries is due both to swollen parasitized endothelial cells of the capillaries and to free " embolic " schizonts.

(*e*) " Stickiness " of the capillary endothelium developed only after the establishment of the infection in the capillaries.

(*f*) The endothelium of the brain capillaries is invaded before that in other organs and tissues.

The paper is illustrated by a coloured plate. *H. E. Shortt*

HAWKING, F. & PERRY, W. L. M. **Activation of Paludrine.** *Brit. J. Pharmacol. & Chemotherapy.* 1948, Dec., v. 3, No. 4, 320–25, 1 fig.

It was found by TONKIN [this *Bulletin*, 1947, v. 44, 184] that paludrine was inactive against the exoerythrocytic forms of *P. gallinaceum* in culture. In view

of the *in vivo* activity it was concluded from preliminary experiments [*ibid*, 1947, v. 44, 648] that the drug was activated by host cells. Further evidence of this activation is now given. Sterilization of cultures was obtained by addition of serum from a fowl treated with paludrine, but none if the drug was added directly unless it were added in a concentration toxic to the cells themselves. LEVADITI and YAMANOUCHI (*C. R. Soc. Biol.*, 1908, v. 65, 23) showed that incubation of atoxyl with rabbit liver rendered this substance active against trypanosomes *in vitro*. Paludrine has been found to be activated by using rat liver. Calculation showed that only a very small amount of the active material formed could have been present in the cultures. ACHESON *et al.* [this *Bulletin*, 1947, v. 44, 964] have shown that the active substance is probably not a benziminazole derivative derivable from paludrine itself. Experiments with the monkey parasite *P. cynomolgi* gave similar results to the above. The authors concluded that paludrine itself is probably not the active antimalarial agent but rather some substance derived from it by the action of body cells. This substance was not bound to protein and was stable at 100°C. *J. D. Fulton*

MICKS, D. W., DE CAIRES, P. F. & FRANCO, L. B. **The Relationship of Exflagellation in Avian Plasmodia to pH and Immunity in the Mosquito.** *Amer. J. Hyg.* 1948, Sept., v. 48, No. 2, 182–90, 1 fig. [16 refs.]

The study which is the subject of this paper was undertaken to investigate the factors underlying the inability of certain species of mosquitoes to act as hosts for various avian malaria parasites, especially *Plasmodium elongatum*. The other species used were *P. cathemerium* and *P. relictum*, while the mosquito species investigated were *Culex pipiens*, *C. quinquefasciatus* [*C. fatigans*], *Aëdes aegypti* and *Anopheles quadrimaculatus*.

Exflagellation preparations were made in two ways and observed at room temperature. In the first method, a drop of bird's blood was mixed with a drop of isotonic saline-citrate solution and the mixture sealed under a coverslip. In the second, the last two abdominal segments were cut off a mosquito immediately after it had fed, the blood was expressed on to a slide and sealed as before.

On the assumption that the hydrogen-ion concentration in the gut might be the important factor concerned in the varying susceptibility of mosquitoes to infection, the *p*H values of the contents of mosquitoes' stomachs were investigated. The Beckman *p*H meter was used and the *p*H values of the stomach contents of both unfed and fed mosquitoes were determined.

In the case of *P. elongatum*, it was noted that exflagellation did not take place in preparations made from the bird's blood but took place readily and rapidly in the contents of the mosquitoes stomach (*C. pipiens*). On the other hand, such exflagellation did not take place when the mosquitoes used were *Aëdes aegypti* and *A. quadrimaculatus*. This seemed to indicate the presence of some factor in the stomach of *C. pipiens* which provoked exflagellation.

It is unnecessary to describe the various other experiments carried out with the species of *Plasmodium* and mosquitoes previously mentioned, but a summary of the conclusions arrived at may be given :—

1. No correlation could be shown between exflagellation and *p*H values.
2. The insusceptibility of a mosquito to infection can manifest itself sufficiently early to prevent even exflagellation.
3. Some chemical factor provoking exflagellation and fertilization of *P. elongatum* is present in the stomach of *C. pipiens*.
4. In the stomachs of *Aëdes aegypti* and *A. quadrimaculatus* a factor inhibiting exflagellation of *P. elongatum* is present.
5. The stimulating factor in *C. pipiens* is activated by the ingestion of blood.

H. E. Shortt

BLACKWATER FEVER

RAOULT, A. Essais de traitement de la fièvre bilieuse hémoglobinurique par Néo-Antergan. [**Treatment of Haemoglobinuric Fever with Neo-Antergan.**] *Bull. Méd. de l'Afrique Occidentale Française.* 1947, v. 4, No. 2, 89–98.

The use of a synthetic anti-histamine preparation, such as neo-antergan, in the treatment of haemoglobinuric fever was suggested by the analogy between the sudden onset of haemoglobinuria, and of other grave complications of malarial attacks, and histamine shock. The author believes that a discharge of histamine is directly responsible for the haemolysis, the natural antihistamine defence of the body being defective, the liver ceasing to play its neutralizing rôle.

A child 8 years of age, infected with *P. falciparum*, developed rhythmic febrile attacks of haemoglobinuria. The usual treatments, including quinacrine, antivenene, calcium, biocholine, and blood transfusions, had failed to arrest the attacks and the progressive anaemia. The child was then given 0·5 gm. of quinoform intramuscularly and 3 tablets of neo-antergan by mouth, at intervals of two hours. The quinoform was continued for 3 more days and the neo-antergan, 3 tablets a day, for a week. Suppression of both haemoglobinuria and albuminuria followed promptly the administration of neo-antergan.

To overcome the difficulty experienced in giving drugs by mouth to patients with haemoglobinuric fever a preparation of neo-antergan suitable for intramuscular injection was prepared for the author. He treated 3 other cases, similar to the first, by intramuscular injections of neo-antergan and quinacrine. In all cases the haemoglobinuria responded promptly to the medication. The subsequent administration of quinine produced no untoward results.

Norman White

BRUZAT & BOUCHET. Anurie au cours d'une fièvre bilieuse hémoglobinurique. Traitement chirurgical. Avant-propos de L. BORDES. [**Surgical Treatment of Anuria during Blackwater Fever.**] *Méd. Trop.* Marseilles. 1948, July–Aug.–Sept.–Oct., v. 8, No. 4, 427–31.

Report of a case which was ultimately fatal.

TRYPANOSOMIASIS

JACKSON, C. H. N. **Some Further Isolated Generations of Tsetse Flies.** *Bull. Entom. Res.* 1948, Dec., v. 39, Pt. 3, 441–51.

Further experiments are reported [see this *Bulletin*, 1946, v. 43, 312] in which tsetse flies are liberated in an area in which they do not naturally occur, and studies made on age, reproduction, etc., under these conditions.

The area chosen for an experiment is judged to be not unsuited to the liberated species, which is therefore living under almost natural conditions. As liberation is from pupae, and is limited to three days, the age of any fly which is subsequently recaptured is known : the distance it has moved from the point of liberation can also be studied. In each experiment tsetse were liberated in a place in which there is already a closely related " native " species : thus *G. morsitans* and *swynnertoni* were liberated in one another's haunts. The general condition of the native community gives a general indication of what the introduced species will encounter.

In the four experiments here discussed (in which *morsitans* and *swynnertoni* were the introduced species), the author compares these flies, using physiological criteria, with others in their native haunts. He also studies their gradual

disappearance, and finds fresh evidence that the males are rather inactive for the first four weeks of life. This modifies previous calculations on length of life in nature, and estimates of population. It seems that the wear and tear of the wing (" wing fray ") proceeds at much the same rate at different seasons, so that it may develop into a means of measuring the mean age of groups of tsetse. Unusually small flies, perhaps the smallest 10 per cent., seldom live long enough to take a meal of blood. Size of offspring depends on the mother's nutrition during pregnancy ; it follows that some apparently minor unfavourable factor might have a marked effect on the numbers in a population of tsetse.

The three larval instars are distinguished, and identified in recaptured specimens of the introduced species, of which the age is known, as explained above. At a screen temperature of 24°C. a large larva has been found in the uterus on the 23rd day. There seemed to be considerable irregularity in the commencement of breeding, but perhaps this was due to the experimental conditions. The first flies of the second generation were captured (soft and unfed) on the 53rd day. *P. A. Buxton*

MOGGRIDGE, J. Y. **Night Activity of Tsetse** (*Glossina*) **on the Kenya Coast.** *Proc. Roy. Entom. Soc. London.* Ser. A. Gen. Entom. 1948, Dec. 28, v. 23, Pts. 10/12, 87–92.

The author has made observations on the adult of *Glossina austeni*, a species which is normally regarded as seldom biting man. He finds that on the Kenya Coast, and especially in the dry season, this insect bites man readily at night. Considerable numbers were caught by a party moving along a path in the bush after midnight carrying no lights. As the insects bite irrespective of the state of the moon and are prepared to do so on a very dark night, the view that their sense of smell is important in finding a host is to some extent strengthened. As soon as day breaks, the attack of these insects on man ceases, except that in very dry weather there is a period of " rush activity " : they then attack man fiercely for a brief period in the very early morning.

P. A. Buxton

LAUNOY, L. Prophylaxie chimique par voie orale, chez le rat, de l'infection expérimentale à *Trypanosoma gambiense* (souche Yaoundé). [**Chemoprophylaxis by the Oral Route against the Yaounde strain of** *T. gambiense* **in the Rat.**] *Bull. Soc. Path. Exot.* 1948, v. 41, Nos. 7/8, 464–70, 4 figs. on 2 pls.

This contribution covers the same ground, with some slight differences of detail, as a recent paper under almost an identical title by the same author [LAUNOY, this *Bulletin*, 1948, v. 45, 1071].

An interesting point mentioned in the present report is that the strain of *T. gambiense* used has retained its infectivity for man after being maintained in laboratory animals for 14 years, as proved by an accidental human infection in Paris in December 1947. *E. M. Lourie*

DEWEY, H. M. & WORMALL, A. **Studies on Suramin (Antrypol, Bayer 205). 6. Further Observations on the Determination of Suramin in Whole Blood and Serum.** *Biochem. J.* 1948, v. 43, No. 1, 24–7. [12 refs.]

Simple methods for the estimation of suramin (Antrypol, Bayer 205) in serum and plasma, by means of acid hydrolysis followed by diazotization, have already been described [this *Bulletin*, 1938, v. 35, 714 ; 1939, v. 36, 668]. In view of the possibility of bacterial contamination in specimens

kept for some time and subsequent production of substances which would vitiate the result of the colorimetric estimations, the effect of addition of various antiseptics to the test specimens has been investigated. In the case of oxalated and defibrinated whole blood or of washed red cells the recoveries of added suramin, in contrast to those with plasma or serum, were low and variable when hydrolysis was carried out for the usual 6 hours, and were not improved by increasing the reaction time. Some constituent of the red cells, or product derived from them, is apparently responsible for the low results obtained. If, however, hydrolysis in those cases is carried out before the addition of suramin satisfactory results are obtained. The amount of suramin which combines with red cells when added to whole blood or as a result of injection in animals is negligible. The addition of 0·2 ml. of 5 per cent. (w/v) phenol or half that amount of 0·5 per cent. merthiolate added to 2 or 3 ml. of plasma or serum did not interfere with satisfactory recoveries of suramin.

J. D. Fulton

GAGE, J. C., ROSE, F. L. & SCOTT, Mary. **The Estimation of Suramin in Plasma.** *Biochem. J.* 1948, v. 42, No. 4, 574–7, 2 figs.

Methods for the estimation of suramin (Bayer 205, Antrypol) have been described in which the acid or alkaline fission products are converted to an azo dye [this *Bulletin*, 1938, v. 35, 714 ; 1948, v. 45, 772]. In the present investigation a method for estimating suramin in aqueous solution, plasma or serum is described, which depends on the colour change produced when the drug is added to a styrylquinoline dye (SQ24). Plasma proteins do not interfere with the formation of the dye complex and the estimation depends on a comparison of optical densities in a Coleman spectrophotometer or a Spekker absorptiometer. The values obtained are referred to a standard curve constructed with known amounts of suramin. The method was compared with that employing the acid hydrolysis referred to above, and is claimed to have equal precision and slightly greater sensitivity. It also proved simpler and less time-consuming and should have advantages in field work. A number of possible hydrolysis products were also estimated by the newer method. It was found that only certain types took part in the formation of the coloured complex and showed a correlation with the time of persistence in the blood.

J. D. Fulton

VAN HOOF, L., HENRARD, C. & PEEL, E. Quelques observations sur les trypanosomiases des grands mammifères au Congo Belge. [**Observations on Trypanosomiasis in Large Mammals in the Belgian Congo.**] *Acta Tropica.* Ba le. 1948, v. 5, No. 4, 327–44. [13 refs.]

(i) CURD, F. H. S. & DAVEY, D. G. **"Antrycide": a New Trypanocidal Drug.** *Nature.* 1949, Jan. 15, 89–90.

(ii) NATURE. 1949, Jan. 15, 77–8. **Sleeping Sickness and Nagana.**

(i) "Antrycide" gives promise of a remarkable degree of activity against *T. congolense*, besides being highly active also against trypanosome species which are normally more amenable than *T. congolense* to chemotherapeutic treatment.

The name "Antrycide" is applicable to the various salts of a bis-quaternary base, whose formula is given, in which substituted pyrimidine and quinaldine rings are connected by an imino linkage.

The following results are given for therapeutic tests in mice with one of the "Antrycide" salts (doses per kgm. body weight, subcutaneously) :—

T. rhodesiense (Tinde) :	25 to 5 mgm. inclusive ; curative.
	Lower doses not quoted.
T. brucei (Liverpool)	5 mgm. ; some cures.
	2·5 mgm. ; blood temporarily cleared.
T. congolense (Busimbi) :	1·0 mgm. ; curative.
	0·5 mgm. ; some cures.
	0·25 mgm. ; blood temporarily cleared.
	0·125 mgm. ; blood sometimes temporarily cleared.
T. evansi (India) :	1·25 mgm. ; curative.
	0·5 mgm. ; some cures.
T. evansi (Sudan) :	2·5 and 1·25 mgm. ; some cures.
	0·5 mgm. ; blood temporarily cleared.
T. equiperdum :	0·5 mgm. ; curative
	0·25 mgm. ; some cures.
T. equinum :	1·25 mgm. ; curative.
	0·5 mgm. ; some cures.

Considerable prophylactic action was demonstrated in mice, rats and rabbits. Thus, 12·5 mgm. per kgm. body weight completely protected mice against *T. congolense* (Busimbi) inoculated 28 days later.

In trials now proceeding in Africa, single doses of "Antrycide" salts have already produced cures of *T. congolense*, *T. vivax* and *T. brucei* infections in cattle, of *T. brucei* in horses, donkeys and dogs, and of *T. evansi* in camels. Considerable protective power has also been demonstrated against *T. congolense* and *T. vivax* infection in cattle.

(ii) This leading article was inspired by the discovery of "Antrycide", referred to in the abstract above. The first public announcement of "Antrycide" was made at a Press conference held jointly by the Colonial Office and Imperial Chemical Industries, Ltd. on December 29, 1948.

The article refers to the severe limitations which tsetse flies have imposed on the development of tropical Africa. Mention is made of some of the methods now in use for controlling trypanosomiasis in man and animals, either by measures directed essentially against the fly or against the trypanosome ; and the large measure of success already achieved is acknowledged. "There are some hundreds of thousands of people, and their cattle, living where they could not have lived before. Still larger numbers have been protected from sleeping sickness by the use of drugs, and now that it is possible to treat cattle themselves, an even larger area will be available for development." A warning is nevertheless sounded against the expectation of producing any immediate and widespread improvements in food-production or human settlement, in view of technical difficulties of dealing with large numbers of cattle which have never been handled and which range over large unfenced areas.

Mention is rightly made of the other important advance of recent years in the chemotherapy of *T. congolense*, namely the introduction of phenanthridinium compounds, culminating in "Dimidium bromide", [reports on which have been conflicting, and the relative value of which has accordingly not yet been finally established]. *E. M. Lourie*

GANAPATI, P. N. **Cultivation of *Trypanosoma cruzi* in the Developing Chick Embryo.** [Correspondence.] *Nature*. 1948, Dec. 18, 963–4, 2 figs.

Tissue culture of *Trypanosoma cruzi* in the embryonic tissues of the chick is readily carried out, but attempts to cultivate this parasite in the chick embryo itself have been less successful. The account given in this note records the

successful cultivation of *T. cruzi* on the chorioallantoic membrane of the chick embryo ; both blood forms and cultural forms were used as the inoculum.

The eggs were used after 10–14 days' incubation and the inoculation was made by the standard technique of Beveridge and Burnet. The eggs were opened from the third day onwards. All the chicks died before hatching.

The lesions on the chorioallantoic membrane were whitish opaque patches. Sections showed that the infection was in the ectodermal layer, which contained numerous " cysts " enclosing large numbers of *T. cruzi* in all stages of multiplication. The mesodermal layer is not involved. *H. E. Shortt*

Pizzi, T., Valls, J. & Florenzano, R. Estudio preliminar sobre la cardiopatia chagasica en la zona central de Chile. [**Preliminary Study of Cardiopathy in American Trypanosomiasis in Central Chile.**] *Rev. Med. Chile.* 1948, June, v. 76, No. 6, 315–23.

The authors examined 411 patients proved by xenodiagnosis to be suffering from Chagas's disease ; 397 electrocardiograms were made and 43 showed definite departures from the normal. Among 66 controls four showed abnormalities, one with blocking of the left ramus (with hypertension and cardiac insufficiency), others were slight alterations in the ST segment and the T-wave. The authors conclude that myocardial affections in this disease are neither common nor severe in the zones investigated ; the most important are A-V block, especially of the right ramus.

As the authors agree, the study is not very complete because they had no portable X-ray apparatus, nor could they make electrocardiograms on all the patients ; on the other hand, controls were few in number, only 66, and they could not be certain that none of them was infected with the disease, since they lived in the same districts as the positive [rather serious drawbacks to the validity of the conclusions]. *H. Harold Scott*

LEISHMANIASIS

Brinkmann, E. Kala-Azar bei einem Heimkehrer. [**Kala Azar in a Repatriate.**] *Deut. med. Woch.* 1948, Aug. 13, v. 73, Nos. 29/32, 348.

A case in an ex-prisoner of war from Tunis.

Bozzo, A. & Canu, G. Su un caso di sepsi lenta da paratifo A in soggetto con leishmaniosi viscerale. [**A Case of Subacute Bacterial Endocarditis associated with Kala Azar.**] *Acta Med. Italica.* 1948, Nov., v. 3, No. 11, 281–5, 1 chart. [14 refs.]

The English summary appended to the paper is as follows :—

" A case of subacute bacterial endocarditis caused by *Salm. paratyphi*, A. in a patient with kala-azar has been presented. The authors call attention to the rarity of this aetiology and to the association of subacute bacterial endocarditis with leishmaniasis."

Tsavaris, B. Le kala-azar au Dodécanèse. Foyers et observations. [**Kala Azar in the Dodecanese.**] *J. Roy. Egyptian Med. Ass.* 1943, Oct., v. 26, No. 10, 357–9. [Recd. 13 Dec., 1948]

Duffy, J. P. & Davison, L. E. **Kala-Azar : 3 Cases developing in Veterans.** *Amer. J. Med. Sci.* 1949, Jan., v. 217, No. 1, 21–7, 6 figs.

Two cases from India and one from Africa, occurring in U.S. ex-servicemen.

CHUNG, Huei-lan, CHOW, Hua-k'ang & LU, Jui-ping. **The First Two Cases of Transfusion Kala-Azar.** *Chinese Med. J.* Shanghai. 1948, June, v. 66, No. 6, 325–6. [10 refs.]

This paper describes the apparent transmission of kala azar to two children by blood transfusion from a mother suffering from the disease. On diagnosis of the mother's condition, made after the transfusions, a close watch was kept on the two children. Kala azar was diagnosed in each after the lapse of nine and ten months respectively.

[There is no reason to doubt that the most probable cause of the disease in the two children was the blood transfusion, since *Leishmania donovani* is constantly present in the blood of untreated cases. None the less, the possibility of transmission by *Phlebotomus* flies from mother to child cannot be excluded in spite of the recorded fact that the premises were " well screened against insects as it was occupied by a well-known parasitologist ". After all, the mother had acquired the infection without blood transfusion.] *H. E. Shortt*

DANA, R., CORCOS, A. & SEBAG, A. Deux cas de kala-azar chez un adulte et chez un enfant guéris par le 2168 R.P. [Glucantime]. [**Two Cases of Kala Azar, an Adult and a Child, cured by Glucantime (2168 R.P.).**] *Bull. et Mém. Soc. Méd. Hôpit. de Paris.* 1948, Nos. 20/21, 644–8, 2 charts.

Two cases of kala azar are reported. One, a young woman aged 27 years from Tunisia, complained of fever with rigors and sweating, weakness, and loss of appetite of about 6 months' duration. Her spleen was four fingers' breadth below the costal margin and the liver was enlarged. *Plasmodium vivax* schizonts were found in the blood. Anti-malarial treatment brought down the temperature for about 8 days, but the fever returned and on this occasion *P. falciparum* parasites were found. Despite further anti-malarial treatment, irregular fever persisted, the spleen now reached to the crest of the ilium, and the liver was four fingers' breadth below the costal margin. The inguinal and axillary lymphatic glands were enlarged. Leishmaniae were found on sternal puncture. The leucocyte count was 630 per cmm. and the haemoglobin 32 per cent.

The patient was treated by " glucantime " (2168 R.P.) intramuscularly, in 15 doses, 5, 5, 6, 8, 10×8, and 12×3 ml.=140 ml. (=11·30 grammes of antimony), on alternate days. The temperature fell after the second injection. After this course, the spleen and liver were reduced to less than half their previous size and the blood picture improved (haemoglobin 58 per cent.). Control sternal puncture was refused, but over 3 months later the patient was reported to be in excellent health with no return to fever.

The second case was in a child of 5 years from Beja (Tunisia), with an oscillating temperature (37·5° to 39°C.), anaemia (62 per cent. haemoglobin), leucopenia (2,100 per cmm.), a large spleen reaching almost to the iliac crest, and an enlarged liver. Leishmaniae were found on sternal puncture. The same drug was given in 15 doses of 2·5, 4, 5×4, and 6×9 ml.=75 ml. [*sic.* ? 80·5 ml.] corresponding to 19·50 grammes of the product (presumably a 25 per cent. solution). The temperature fell and remained below 37°C. after the 4th injection, the spleen and liver were reduced, and the leucocyte count rose to 5,500 per cmm. after one month. Sternal puncture was now negative. The child, still in excellent condition, was readmitted after three weeks and given a second similar course of 15 injections totalling 88 ml.

The authors emphasize : (i) the danger of overlooking kala azar in patients with malaria, especially when the splenomegaly persists after the temperature has fallen, and (ii) the excellent results they obtained with glucantime (2168 R.P.).

[There is no information on the formula of 2168 R.P. but from its dosage and antimony content it might be identical with sodium antimony gluconate.]
L. E. Napier

Ho, E. A., Hsu, Tze-hui & Li, Y. **A Report on Examination of 994 Dogs in Sian and its Nearby Villages for Leishmaniasis.** *Chinese Med. J.* Shanghai. 1948, July, v. 66, No. 7, 387–9. [11 refs.]

" Four of 488 dogs examined in Sian were found to have visceral leishmaniasis with cutaneous manifestation, but among 506 dogs examined in 47 nearby villages none showed the infection."

Cangelosi, G. Contributo allo studio della leismaniosi cutanea. [**Cutaneous Leishmaniasis.**] *Giorn. di Med. Milit.* 1948, Mar.–Apr., v. 95, No. 2, 127–9.

Much has been compressed into a small space in this concentrated account of the treatment of cases of cutaneous leishmaniasis. The figures throughout are given as percentages—a little inclined to mislead when the totals dealt with were 31, 29 and 25 in different parts of the contribution.

Of the 31 Italian prisoners of war under the author's care and suffering from oriental sore, 23 came from the Province of Gondar, 4 from Cyrenaica, and 2 each from Eritrea and Asmara [stated as 75 per cent. of cases coming from Gondar Province]. There was none from Somalia or southern Ethiopia. The incubation period, *i.e.* the time between leaving the infective area and the appearance of symptoms, was 2–5 months in 24 per cent. [7 or 8 patients ?], 7–12 months in 32 per cent. [10 ?], 12–24 months in 24 per cent., 24–36 months in 16 per cent., over 36 months in 4 per cent. [1 or 2 ?] ; the longest period was one of 37 months.

Several methods of treatment were tried : trivalent antimony, intravenously and intramuscularly, with fouadin and anthiomaline ; pentavalent stibosan intramuscularly, stibenylurea intravenously, all without benefit. Local infiltration with anthiomaline was equally ineffectual. In 4 patients, good results were obtained with antimony ointment or urea-antimonyl 2 per cent., cure resulting in 60, 62, 30 and 20 days. Local injections of emetine proved very serviceable, but it cannot be used near the eyes, as it sets up a violent conjunctivitis. Atebrin [mepacrine] injections brought about cure in a month and a half in 4 patients with oriental sores ranging in size from that of a chickpea to a kidney bean. Those in whom the lesion was extensive, ulcerated and lupoid were more resistant. Of 25 such, 10 [stated as 40 per cent.] were cured in 45–80 days, 4 [16 per cent.] in 80–110 days, 5 apparently cured relapsed, but were definitely cured by a second course of the atebrin injections. Resistance to atebrin treatment is ascribed to local conditions, because in the same patient one sore might rapidly clear up while another would again and again relapse. In the remaining 6, relapse persisted in spite of repeated injections. In 4 of these, satisfactory results followed the application of sulphamide in powder, after cleaning and deep scraping of the ulcer. The powder was applied " at first every day, then every second, third and fourth day " [no other details are given] ; cure was obtained in 29, 30, 30 and 45 days. *H. Harold Scott*

Peña Chavarria, A., Ovares Arias, J. C., Romero López, A., Fallas Diaz, M. & Castro Jenkins, A. Leishmaniosis tegumentaria en Costa Rica. Se propone una clasificación dermatológica de la leishmaniosis tegumentaria. [**Cutaneous Leishmaniasis in Costa Rica. A Proposed Classification according to the Skin Lesions.**] *Rev. Med. Costa Rica.* 1946, July–Dec., v. 7, Nos. 147/152, 66–97, 24 figs. & 1 map. [89 refs.]

Cutaneous leishmaniasis is endemic in Costa Rica ; cases can be seen at all seasons, but increase in number with the wet season and mostly at the levels

of some 700 metres above sea-level. *Phlebotomus* abounds in all the affected regions.

In this article, 100 cases are analysed : 54 from the Province of Limón, 20 from Alajuela, 16 from San José, 5 from Guanacaste, 2 each from Cartago and Puntarenas and one from Heredia. As regards sex, the authors state that men are more attacked than women [but no other reference is made to the sex and a tabular statement gives " 86 males, 84 females," an obvious mistake in a total of 100 patients]. Clinical forms are divided into : 1, those with rupial ulcers (*úlcero-costrosas*), much the most numerous (84) ; 2, vegetating and rupial (7) ; 3, affecting the legs only (5) ; 4, vegetating lesions only (3) ; raised papule (*botón*) (1). [Not a very satisfying classification. There are other errors in the table than that referred to above. In the table, analysing 100 cases is the statement, giving the ages : " Children under 1 year, 18 ; to 10 years, 4 ; and 10 to 80 years, 96, a total of 118.] *H. Harold Scott*

Pessôa, S. B. & Villela, F. F. Estudos sôbre o tratamento da leishmaniose tegumentar americana pelo eparseno. [**On the Treatment of American Cutaneous Leishmaniasis by Eparseno.**] *Hospital.* Rio de Janeiro. 1948, Oct., v. 34, No. 4, 527–32.

Eparseno (dioxy-diamido-arsenobenzol) is put up in 1 cc. ampoules each containing 0·12 gm. of amino-arseno-phenol and is given intravenously. In 1926, Pupo reported the results of its use in muco-cutaneous leishmaniasis [see this *Bulletin*, 1926, v. 23, 586]. It has usually been given at 2–3-day intervals for adults, in a series of 10–15 ampoules, repeating the course after an interval of 10–15 days and so on until 40–50 ampoules, or 4·8–6 gm. of the salt have been given.

In the present communication, the authors report having tried two methods. In the one they give increasing doses beginning with one ampoule, then increasing at two-day intervals to 2, 3, 4 and in one case 5 ampoules for a single dose, with a resting period of 3–5 days after the third or fourth injection. For example, one patient received on January 4th 1 cc., January 6th 1 cc., January 8th 2 cc., January 12th 2 cc., January 17th 3 cc., January 22nd 3 cc., then a rest for 10 days [so stated, but the dates would show a rest for 13 days] February 4th 3 cc. and the same dose on the 6th, 8th, 11th, 15th, 18th and 22nd, altogether 33 ampoules or 3·96 gm. of the salt.

Of 15 patients so treated, six showed toxic signs, four of them severe, but cicatrization occurred ; two relapsed.

By the other method the dose was kept constant at 1 cc., but injections were made daily for 10 days, then after an interval of 10–15 days a repeat and so on until 40–50 ampoules had been given. Eight patients were treated in this way. Six were cured, a seventh relapsed 8 months later ; in the other cicatrization was incomplete and the treatment was changed for antimony. None showed any signs of intoxication and the authors consequently regard the second plan—daily administration of the constant dose—as the better. *H. Harold Scott*

FEVERS OF THE TYPHUS GROUP

Erzin, N. Ikinci dünya savasi yillarinda yurdumuzun tifüs durumu. [**Typhus Fever in Turkey in Years of World War II.**] *Türk Ijiyen ve Tecrübi Biyoloji Dergisi.* Ankara. 1948, v. 8, No. 3, 5–9, 1 chart. English summary 10–12.

An epidemic of typhus occurred in Turkey in 1942 and reached its peak in 1943–44. A reduction in the number of cases to pre-war level did not occur until 1947.

The average incidence and mortality in the 10 years before the war (1928–1938), the 4 years up to 1942, and from 1943 to 1947 are shown in a series of tables.

The average number of cases in the 10-year period 1928–1938 was 211 ; in 1939–1942, 759 ; and from 1943 to 1947, the actual numbers were 4142, 3251, 2654, 1496 and 641.

It is shown that most of the cases occurred between January and May, and particularly in March. This is attributed by the author to lack of communications, which limits the spread of the disease in the winter months.

The incidence of typhus and death rates per 100,000 for different periods were as follows :—

	Incidence		Death rate	
	Number	Average per 100,000	Number	Average per 100,000
1935–39	475 (yearly average)	2·9	58 (yearly average)	0·3
1940–44	2,003 ,, ,,	11·2	189 ,, ,,	1·0
1945	2,654	13·8	139	0·7
1946	1,496	7·8	103	0·5
1947	641	3·4	56	0·3

The fall in incidence from 1944 onwards is attributed largely to mass vaccination and the use of DDT. Mass vaccination was begun in 1943 and another table shows that the mortality rate from typhus fell from 14·1 in 1942 to 5·0 in 1945 (but rose to 6·8 and 9·0 in the next two years). The incidence of typhus as a percentage of other common infectious diseases rose from an average of about 4 between 1935 and 1942 to about 14 between 1943 and 1946.

H. J. O'D. Burke-Gaffney

Ferro-Luzzi, G. Studio sulle malattie del gruppo del dermotifo in Eritrea. [**Studies of the Fevers of the Typhus Group in Eritrea.**] *Boll. Soc. Ital. di Med. e Igiene Trop.* (Sez. Eritrea.) 1948, v. 8, Nos. 3/4, 110–45, 9 figs. (7 on 4 pls.). [57 refs.] English summary.

The author gives an interesting summary of the numerous observations made by various Italian workers on the fevers of the typhus group in Eritrea. During the 10-year period 1927–1936, the total number of cases treated at the Asmara Hospital was 37, of which 28 were in Europeans. In 1937, the number of European patients admitted suddenly rose to 35 and in 1938, 24 European and 25 African patients were admitted.

The progress of the epidemic from 1939 onwards can be judged from the following figures of admissions of African patients : the fatality rates for all patients for each year are given in brackets.

In 1939 there were 152 cases (14·8) ; in 1940, 66 (9·8) ; and in 1941, 320 (14·8). The admissions rapidly fell to 39 (2·2) in 1943 and again rose steeply to 1,084 (11·9) in 1946. The figure for 1947 was 395 (5·1).

In the years of high prevalence the disease was predominantly of the epidemic type, but murine typhus was in evidence throughout the period. Tick-borne typhus was relatively negligible in incidence ; the author is inclined to regard all the cases as having been of the *boutonneuse* type though he states that other workers believe that some of them were of the tick-bite fever type. He describes the chief features of the tick-borne fever as including the occurrence of a *tache noire* and a papulo-nodular rash which is rarely haemorrhagic and

which extends to the palms, soles and face ; the Weil-Felix reaction is inconstant or delayed, and the titres of agglutination of *Pr. OX19* or *Pr. OX2* are low.

In the section dealing with treatment, the author repeats his claim that aspirin in daily quantities of 6–8 gm., continued till defervescence, has caused a fall in fatalities from 14·8 per cent. to 1·0 per cent. In a footnote he takes strong exception to the suggestion by the present reviewer that his methods of control may not have been satisfactory and renews his assertion that when cases were selected the more severe were chosen for the trials of the drug. [See this *Bulletin*, 1948, v. 45, 249.] [One of the present reviewer's comments can now be withdrawn ; this was " it also appears that the same group of patients formed the controls for tests of aspirin and three other drugs." This was based on the fact that exactly the same fatality rate was given for the controls of all the four drugs, but it is now explained that really there were four sets of controls and that the fatality rates were so uniform that an average figure was adopted for convenience. The other comments still seem to the reviewer to have been justified by the facts as stated ; they were not intended to throw doubts on the good faith of the author and in any case they are now rendered obsolete by the further evidence supplied in the present paper, which follows.]

In a further set of trials of aspirin between January 1st and June 30th, 1947, the fatality rate among 74 treated patients was 5·4 per cent. and among 112 controls it was 10·7 per cent. These figures are in striking contrast to those given for the earlier trials in which the corresponding fatality rates were 1·0 per cent. and 14·8 per cent. in the second half of 1947, the fatality rate among 221 treated patients was only 2·26 per cent. ; there were no controls. It would seem reasonable to suggest that there may have been a decline in the severity of the disease during the second half of 1947.

The author makes the interesting suggestion that the action of aspirin may be associated with the benzoic radical which is, perhaps, related to that of para-aminobenzoic acid. *John W. D. Megaw*

Dreguss, M. & Farkas, E. **Complement-Fixation Test for Serological Studies in Typhus Fever.** *Arch. f. d. Gesamte Virusforschung.* Vienna. 1948, June 30, v. 4, No. 1, 47–54. [12 refs.]

This paper describes work carried out in 1944 when the authors had no access to the reports of similar investigations carried out by Bengtson, Topping, Fulton, and other workers.

Among 36 sera of healthy or syphilitic persons there was no case of a positive reaction with the complement-fixation or Weil-Felix tests.

Among 110 sera of patients believed or suspected to have attacks of typhus or typhoid fever there was a general agreement between the results of the two tests, but 13 sera were negative with the Weil-Felix test and positive with the complement-fixation test at titres of 1–16 or over ; in 8 of these cases, later examinations were made and high-titre Weil-Felix reactions were observed.

In 4 cases there was a positive Weil-Felix reaction and an absence of complement-fixing antibodies ; in these the former reaction " seems to be unspecific "; the final diagnosis in two was typhoid fever, in the other two there was no change in the Weil-Felix titres of later samples.

From the results of a number of tests, including those carried out repeatedly on eight patients, the authors conclude that the complement-fixation reaction becomes positive about two days earlier than the Weil-Felix reaction [they seem to have regarded fixation titres of 1–16 as positive and Weil-Felix titres below 1–100 as negative.]

In a group of 10 persons the rise in titre resulting from vaccination was more pronounced with the fixation test than with the Weil-Felix test in all but two cases. *John W. D. Megaw*

DREGUSS, M. & FARKAS, E. **Estimation of the Antigenic Value of Typhus Vaccines by Complement-Fixation Tests.** *Arch. f.d. Gesamte Virusforschung.* Vienna. 1948, June 30, v. 4, No. 1, 55–62.

This paper, like the preceding one, was greatly delayed in publication. The studies described were carried out in 1944–45.

The complement-fixation test as performed by the authors was found reliable as a means of estimating the immunizing value of typhus vaccines.

Among 13 vaccines of various kinds, and from different sources, only 5 were found satisfactory. Three of these were of the yolk-sac type, one was a mouse-lung vaccine and the fifth was a Weigl louse vaccine. One of the yolk-sac vaccines and the Weigl vaccine were prepared in Hungary; the other two yolk-sac vaccines were of American origin and were the only samples obtained from that source.

Among the eight unsatisfactory vaccines five were of the yolk-sac type, the other three were prepared from chick embryos, mouse lungs and rabbit lungs, respectively. Three out of the four vaccines originating from state-controlled institutions in European countries other than Hungary were unsatisfactory, so also were all the three described as "manufactured and marketed in Europe." The age and conditions of storage of most of the vaccines were unknown. *John W. D. Megaw*

ZIA, S. H. & CHANG, N. C. **Studies of Typhus Fever in Peiping by the Complement Fixation Test.** *Proc. Soc. Exper. Biol. & Med.* 1948, Oct., v. 69, No. 1, 22–3.

Among 20 sera of patients suffering from typhus fever in Peiping only one gave a higher-titre reaction with murine than with epidemic antigen in complement-fixation tests; five gave equal titres with both antigens, 13 gave titres twice to four times higher with epidemic antigen and one reacted only with epidemic antigen, at a titre of 1–640.

The interesting feature of these results is that the authors in previous studies had tended to regard the rickettsiae of human typhus in Peiping as being predominantly of the murine type. They now state that the results of the fixation tests suggest that the rickettsiae, both in the autumn and spring of the past two years, were largely of the epidemic type. In their previous studies they had relied on biological tests. [See, for example, this *Bulletin*, 1942, v. 39, 143, 144, and 613.] *John W. D. Megaw*

WESTERN AUSTRALIA. **Report of the Commissioner of Public Health for the Year 1947** [COOK, C. E.]. 66 pp., 1 chart. 1948. Perth: W. H. Wyatt, Govt. Printer.

This report contains two points of special interest to readers of the *Bulletin*. Firstly, 141 cases of murine typhus were reported during the year: 52 occurred in the Health area of the Perth Municipality, 70 in other Metropolitan areas and 19 from other parts of the State.

It is noted that 7 per cent. occurred in persons under 15 years, 73 per cent. between 15 and 49 and 20 per cent. in those of 50 years or over. The preponderance of cases during working ages suggests that the place of employment, rather than the home, is the usual source of infection. The aetiology of the

disease takes on a special importance owing to the frequency of claims being submitted by patients under the Workmen's Compensation Act. It is noted that during the year discussions took place regarding the planning of an epidemiological research into murine typhus in Western Australia, with a view to approaching appropriate bodies for a grant.

During the year, 133 specimens of serum were positive to the Weil-Felix reaction (*Proteus X*19) in a titre of 1/100 or over, as compared with 68, 86 and 100 in the previous three years. Monthly incidence of these results is shown in a table : broadly speaking, incidence rose from February to April.

The second point relates to leprosy. It is noted that in 2,210 films from 615 patients, there were 555 which showed acid-fast bacilli.

In 1946, 441 smears were positive out of 1,947 and in 1939, all of 5 smears were negative. *H. J. O'D. Burke-Gaffney*

RICKARD, E. R. **Complement Fixation in Human Sera following Murine Typhus.** *Proc. Soc. Exper. Biol. & Med.* 1948, Oct., v. 69, No. 1, 31–4.

The author carried out careful complement-fixation tests on the sera of 404 persons known or suspected of having suffered from murine typhus fever in Florida. In one group of 203 persons the diagnosis was regarded as highly probable and positive reactions occurred in about 86 per cent. of the sera. In the other group, of 201 persons, the diagnosis was less probable and the reactions were positive in about 64 per cent. Taking account only of the positive reactions, the average titre in each group was almost the same, 1–21 and 1–22, respectively.

The average titre in a group of 67 persons who had been attacked 12 to 23 months previously was 1–30 ; in a group of 123 attacked 24 to 35 months previously it was 1–18 ; and in a group of 94 attacked 36 to 47 months previously it was also 1–18. It appeared, therefore, that there was little tendency to diminution of the titre after two years.

A group of 20 inmates of a New York correctional Institution served as a control ; there were only three positive reactions and all these were at a titre of 1–2. *John W. D. Megaw*

HILL, E. L. & MORLAN, H. B. **Evaluation of County-Wide DDT Dusting Operations in Murine Typhus Control.** *Pub. Health Rep.* Wash. 1948, Dec. 17, v. 63, No. 51, 1635–53, 8 figs. [10 refs.]

The authors describe a large-scale experiment planned for the purpose of finding whether murine typhus could be controlled by dusting rat runs and hiding places with 10 per cent. DDT powder.

Three well-defined rural areas in South-West Georgia were selected in two of the areas, with populations of about 20,000 and 10,000 respectively, organized dusting operations were carried out on five occasions between April 1st 1946 and September 30th 1947. The third area was kept as a control. The numbers of cases of murine typhus in the dusted rural areas in each of the years 1945, 1946, and 1947, were 86 ; 31 ; and 6 ; respectively. The corresponding numbers in the control area were 31 ; 37 ; and 26. Equally significant reductions were observed in the dusted areas with regard to the percentage of rats showing positive complement-fixation reactions against murine rickettsial antigens, and the degree of infestation of the rats with *Xenopsylla cheopis* and *Leptopsylla segnis*.

There was only a slight degree of reduction in the rate of rat infestation by *Liponyssus bacoti* and *Polyplax spinulosa*.

Full details of the experiment are given in the paper which is likely to become a classic on the subject of the control of infections transmitted from rat to man by fleas.

It appears that the heavy dustings employed caused some deaths among the rats and also gave rise at first to mass exodus of the rats from the dusted localities.

John W. D. Megaw

Le Gac, P. Nouveaux cas de fièvre exanthématique au Togo. [**Two Further Cases of Typhus Fever in Togo.**] *Bull. Soc. Path. Exot.* 1948, v. 41, Nos. 9/10, 604–13, 1 chart. [10 refs.]

One of these two cases of typhus-group fever is of special interest in being a striking example of the perplexities that arise in connexion with the interpretation of serological findings ; these were as follows :—

Day of Illness	Weil-Felix titres			Rickettsia-Agglutination titres	
	Pr. OX19	*Pr. OX2*	*Pr. OXK*	Epidemic	Murine
18	100	500	50	40	0
22	100	100	200		
27	50	0	50		
31				100	200
38	50	50	50		
45	200	200	100	100	200
52				40	100
				40	0

Complement-fixation tests, carried out on an unstated day, were positive at a titre of 12·5 with epidemic antigen, and negative with murine and tick-bite fever antigens.

Guineapig inoculations were carried through 32 passages ; the febrile reaction lasted 10–14 days ; there was no scrotal reaction ; 70 per cent. of the animals died and the autopsy findings are said to have resembled those described by some workers as occurring in scrub typhus. No mention is made of the microscopic characters of the exudate.

The author states that the findings are rather disturbing [*troublantes*] and that they tend to strengthen his formerly expressed opinion that the typhus of the African " savannahs " is nearly related to scrub typhus.

The rash was maculo-papular ; a few macules were seen on the hands ; there was no eschar.

There is no mention of the epidemiological conditions in which the infection was contracted.

John W. D. Megaw

Bailey, C. A., Diercks, F. H. & Proffitt, J. E. **Preparation of a Serological Antigen and a Vaccine for Experimental Tsutsugamushi Disease (Scrub Typhus).** *J. Immunology.* 1948, Nov., v. 60, No. 3, 431–41, 3 figs. [15 refs.]

The authors give full details of a method by which they have succeeded in preparing potent suspensions of *Rickettsia tsutsugamushi*. The process involves repeated differential centrifugation of homogenized yolk-sac cultures diluted in casein hydrolysate solutions.

Three strains of the organism were used and all of them yielded suspensions which showed a high degree of activity in fixing complement and in immunizing

guineapigs. Among the six strains of antisera used in the tests antigenic differences similar to those described by other workers were found to exist, but there was evidence of the presence of a common antigen, variable in amount, in all the strains.

Further work to detect the degree of protection afforded to vaccinated animals against heterologous strains is being carried out and will be described in a later paper. *John W. D. Megaw*

DE MAGALHÃES, O. & ROCHA, A. Contribuição para o conhecimento do tifo exantemático neotrópico no Brasil. [**A Contribution to the Knowledge of Neotropical Exanthematic Typhus in Brazil.**] *Mem. Inst. Oswaldo Cruz.* 1947, Dec., v. 45, No. 4, 825–45, 12 graphs. English summary (7 lines).

In their study of neotropical typhus [tick-borne typhus of the Rocky Mountain spotted fever type] in Brazil the authors were struck by the pronounced tendency of infection to occur in small widely separated patches, and they suspected that this distribution might be due to the presence of infection in animals capable of long-range travel such as goats and deer. A goat, a kid and a deer (*Cervus axis*) were found susceptible to intraperitoneal inoculation with the infection so that they were regarded as potential natural reservoirs of the disease.

Weil-Felix tests were carried out on these and other infected animals, including a rhesus monkey, two coatis (*Nasua narica*), two wild cats, a rabbit, and a ferret ; also in a number of uninoculated kids from various areas in Brazil and on three dogs. Nine different strains of proteus were used in the tests—an H and an O strain of *Proteus X19*, *Pr. X2*, *Pr. XL* and *Pr. XK*, and a strain of *Pr. vulgaris*.

The results of the tests are shown in graphs : from these it appears that the responses were of many different types, and the authors state that they have found the same strain of infection to give rise to a great variety of responses in different animals of the same species. *John W. D. Megaw*

TAYLOR, D. J., MULRENNAN, J. A. & THURMAN, D. C., Jr. **Species of Ticks associated with Rocky Mountain Spotted Fever Cases in Florida.** *J. Econom. Entom.* 1948, Oct., v. 41, No. 5, 809–11.

" On the basis of circumstantial evidence presented, *Dermacentor variabilis* appears to be the most likely vector of spotted fever in Florida. The occurrence of *Amblyomma americanum* at the scene of one of these cases is not to be overlooked in view of recent discoveries."

RODRIGUES, P. M. & TRAVASSOS, J. A reação de Bengtson no diagnóstico da febre maculosa das montanhas rochosas. [**Bengtson's Reaction in the Diagnosis of Rocky Mountain Spotted Fever.**] *Hospital.* Rio de Janeiro. 1948, July, v. 34, No. 1, 55–69, 1 graph. English summary. [22 refs.]

Complement-fixation tests carried out by Bengtson's method were employed in the diagnosis of 10 cases of tick-borne typhus in San Paulo. The test was found to be strictly specific in every case and the results obtained with antigens of local origin were identical with those obtained with an antigen supplied from the Rocky Mountain Laboratory, Montana. These results furnished additional evidence of the identity of the spotted fevers of the Rocky Mountains and of San Paulo.

Five of the cases were fatal ; in four of these, sera were examined on the 5th to the 9th day and all were positive, whereas only one was positive with the

Weil-Felix test. Sera of six patients giving titres ranging from 1–8 to 1–128 with the homologous antigen were completely negative with antigens prepared from epidemic and murine strains of rickettsiae. *John W. D. Megaw*

FRASER, L. E., ROSENBLUM, H. & DANCIGER, J. A. **Para-Aminobenzoic Acid in Treatment of Rocky Mountain Spotted Fever.** *Amer. J. Dis. Children.* 1948, Apr., v. 75, No. 4, 493–504, 1 chart. [Refs. in footnotes.]

Details are given of four cases of Rocky Mountain spotted fever in children who were treated with *para*-aminobenzoic acid. In three of the cases, treatment was started on the 8th or 9th day, and rapid improvement was observed. In the fourth case, the first dose was given on the 13th day, but death followed seven days later ; this child, aged seven years, received altogether 144 gm. of the drug, and an excessive blood level of 262 mgm. was reached at one stage, accompanied by extreme acidosis.

The authors do not agree with the observers who claim that the drug is of low toxicity ; they mention in a foot-note that some manufacturers are now producing a sodium salt of the drug which does not appear to cause acidosis.
John W. D. Megaw

HARRELL, G. T., MEADS, M. & STEVENS, K. **"Aureomycin," a New Orally Effective Antibiotic. Clinical Trial in Rocky Mountain Spotted Fever, Results of Susceptibility Tests and Blood Assays using a Turbidimetric Method.** *Southern Med. J.* 1949, Jan., v. 42, No. 1, 4–12, 4 figs.

In the three cases described, aureomycin appears to have had a strikingly curative action similar to that observed in the larger series of cases reported in the following paper.

The total daily oral dosage was 3·0 to 6·0 gm. given in divided doses every four to six hours.

It is mentioned that the drug rapidly loses its activity when kept in solution, even for a few hours. *John W. D. Megaw*

ROSS, S., SCHOENBACH, E. B., BURKE, F. G., BRYER, M. S., RICE, E. C. & WASHINGTON, J. A. **Aureomycin Therapy of Rocky Mountain Spotted Fever.** *J. Amer. Med. Ass.* 1948, Dec. 25, v. 138, No. 17, 1213–16, 1 chart. [Refs. in footnotes.]

This paper opens with a brief summary of what is known with regard to aureomycin, a new antibiotic derived from a strain of *Streptomyces aureofaciens*, which gives rise to a golden colour in culture media.

The drug was found to protect mice and guineapigs against harmful results from inoculation with the rickettsiae of Q fever, rickettsialpox, Rocky Mountain spotted fever, and murine typhus. The drug is readily absorbed when given by the mouth and is of low toxicity except when administered intravenously. Doses up to 60 mgm. per kgm., daily *per os*, cause no toxic effects except occasional nausea and vomiting after the first few doses. References are given to five papers presented at a conference on Aureomycin held under the auspices of the New York Academy of Science on July 21st 1948.

In the present study, 13 patients with Rocky Mountain spotted fever were treated. The ages of the patients ranged from 16 months to 50 years.

The results are described in detail ; they were remarkably good, and appear to resemble closely those described by SMADEL *et al.* as occurring in cases of scrub typhus treated by chloromycetin [this *Bulletin*, 1949, v. 46, 27].

The average duration of the fever after the first dose was two-and-one-third days ; and even in the two patients whose treatment started on the 8th day

of the illness the response was equally satisfactory, whereas in a previous series of cases treated with *para*-aminobenzoic acid no benefit was observed among patients whose treatment started after the 7th day.

The dosage adopted was : three initial doses of 2–5 mgm. per kgm., *per os* at intervals of one hour ; then the same doses every two hours till the temperature had remained normal for two days ; then the same doses every four hours. The duration of treatment ranged from four-and-a-half days to nine days ; the average total amount of the drug was 9·5 gm., the range being 2·3 to 16·3 gm.

In all the cases that came under treatment before the 7th day there was a striking absence of symptoms pointing to the need for supportive treatment.

No mention is made of the availability or cost of the drug.

John W. D. Megaw

Ortiz Mariotte, C. & Calderón, C. Hexaclorocicloexano, su efecto en la garrapata común del perro en México. Prueba de laboratorio—Informe preliminar. [**The Effects of Hexachlorocyclohexane on Dog Ticks in Mexico.**] *Bol. Oficina Sanitaria Panamericana*. 1948, Aug., v. 27, No. 8, 719–23. English summary.

The commonest dog tick in Mexico is *Rhipicephalus sanguineus*, which abounds in the northern States, where it is considered to be an important vector of Rocky Mountain spotted fever [this *Bulletin*, 1946, v. 43, 1134 ; 1948, v. 45, 165, 252]. The authors describe a number of experiments indicating the lethality of gammexane to ticks. The advantages of this substance and its comparative absence of toxicity to domestic stock suggest that it may enable the control of "spotted fever" to be achieved. Satisfactory results were obtained with DDT in La Laguna in 1947, and the authors suggest that comparative studies be made in areas of Mexico where *R. sanguineus* is prevalent, to ascertain the relative practical and economic values of DDT and gammexane in controlling this vector of the disease. *H. J. O'D. Burke-Gaffney*

Heni, E. & Germer, W. D. Q(ueensland)-Fieber in Deutschland. [**Q(ueensland) Fever in Germany.**] *Deut. med. Woch.* 1948, Oct. 15, v. 73, Nos. 39/40, 472–6, 5 figs.

In September 1947, the author began to observe the occurrence, in villages near Tübingen, of an influenza-like illness in which a considerable number of the patients had symptoms of atypical pneumonia.

A detailed study was made of an outbreak of the disease at Remmingsheim, a compact farming community of about 700 persons. The first cases occurred at the end of November, and no less than 260 persons were attacked during the month of December. By the beginning of February 1948, the outbreak came to an end. The total number of cases was 326.

The first serological tests were carried out in January ; among 21 sera 19 gave positive complement-fixation reactions against Q fever antigen, at titres ranging from 1–32 to 1–1,024. At a later stage 13 other cases were confirmed by complement-fixation tests of patients' sera or of inoculated guineapigs. The 32 proved cases belonged to 28 families of whose members 100 were attacked.

A detailed clinical description of the disease is given : the only special feature was that altogether seven patients died. Two of the deaths were due to pulmonary embolism ; one to a metastatic empyema following gangrene of both feet : the remaining four fatalities occurred in old men who developed hypostatic pneumonia after mild attacks. Radiographic evidence of lung involvement

was found in 23 per cent. of the cases. The severity of the attacks was extremely variable ; ambulatory or very mild cases occurred more frequently among women and children than among men.

A brief description is given of outbreaks in three other villages near Tübingen during 1948. In one village of 1,450 inhabitants there were about 300 cases ; in another with a population of 4,000 it was estimated that 30 per cent. of the people were attacked.

Most, but not all, of the patients had been associated with cattle ; inhalation of dust derived from dried faeces of infected ticks ; the drinking of infected milk ; and man-to-man infection by inhalation of infected droplets were possible modes of transmission. The last-mentioned method would best account for the explosive nature of the outbreaks and the spread of infection through whole families, starting from a single infected person.

Some confusion resulted from the simultaneous occurrence of another short fever in which also atypical pneumonia often occurred ; this appears to have been a true virus infection ; the catarrhal symptoms were more pronounced, and attacks in infants were much more common than was the case with Q fever. The only reliable method of diagnosis was the complement-fixation test.

John W. D. Megaw

PAYZIN, S. Orta anadolu'da bir köyde Q hümmasi salgini. [**Q Fever Epidemic in Ozancik Village.**] *Türk Ijiyen ve Tecrübi Biyoloji Dergisi.* Ankara. 1948, v. 8, No. 3, 116–23. English summary 124–5.

——. Fas, Ankara, Izmir çikägli Q hummasi suşlari ile bağişiklik deneyleri. [**Cross Immunity Experiments with Original Maroc, Ankara, Izmir Q Fever Strains.**] *Ibid.* 126–9. English summary 130–31.

The epidemic described occurred in a village of Anatolia ; there were 20 cases in one of which there was a typhus-like rash.

Rickettsia burneti was isolated by guineapig inoculation ; one strain was isolated and identified by R. R. PARKER from a tick (*Ornithodorus lahorensis*) which had fed on an infected guineapig.

Infection was suspected of having been transmitted by the inhalation of infected dust from wool kept in the houses of the patients. Apart from this outbreak it is stated that many strains of *R. burneti* have been isolated from patients in many parts of Turkey, where the disease is endemic. Guineapigs convalescent from experimental attacks were found immune to a Morocco strain, to two Smyrna strains, and to an Ankara strain.

John W. D. Megaw

BROWN, D. C., KNIGHT, L. A. & JELLISON, W. L. **A Fatal Case of Q Fever in Southern California.** Reprinted from *California Med.* 1948, Sept., v. 69, No. 3, 3 pp.

" The first confirmed fatal case of Q fever in Los Angeles County is reported. The patient's occupation brought him in frequent contact with livestock (a characteristic of about 72 per cent. of the cases so far studied in Southern California). The clinical course was typical of the disease. The patient was the first under 50 years of age known to have died of Q fever. The clinical history and the gross and microscopic pathological findings were consistent with those of a previous fatal case in America. The diagnosis was confirmed by the isolation of *C. burneti* in experimental animals injected with blood and sternal marrow collected at postmortem examination."

JELLISON, W. L., ORMSBEE, R., BECK, M. D., HUEBNER, R. J., PARKER, R. R. & BELL, E. J. **Q Fever Studies in Southern California. V. Natural Infection in a Dairy Cow.** *Pub. Health Rep.* Wash. 1948, Dec. 10, v. 63, No. 50, 1611–18.

A detailed examination was carried out on the carcase of a dairy cow slaughtered while excreting rickettsiae of Q fever in her milk, and while positive at a titre of 1–32 with the complement-fixation test against Q-fever antigen. There was evidence that infection had been present for at least two months. The cow was in the fifth month of pregnancy.

Full details are given of the gross and microscopic changes detected in the various tissues, but the authors conclude that none of these changes can with certainty be attributed to infection with Q fever.

The changes include a subacute and chronic focal mastitis and a slight degree of focal cellular infiltration of the kidneys, lungs, and pituitary body.

An extensive series of inoculation tests were carried out on guineapigs; suspensions were made of all the important organs of the body; the only ones found definitely infected were eight made from different parts of the udder and one from a supramammary lymph node. One out of four guineapigs inoculated with lung suspension became infected, but a further test, in which eight guineapigs were inoculated with other lung suspensions, gave negative results. Milk from each of the four quarters of the udder was infected. Blood and other fluids of the cow and the unborn calf gave negative results.

The evidence of infection in the experimental guineapigs was the appearance in their sera of complement-fixing antibodies against Q-fever antigens.

John W. D. Megaw

LACKMAN, D. & PARKER, R. R. **The Serological Characterization of North Queensland Tick Typhus.** *Pub. Health Rep.* Wash. 1948, Dec. 10, v. 63, No. 50, 1624–8.

In the present study, 30 rabbits were inoculated intraperitoneally with a strain of rickettsia originally isolated from a case of North Queensland tick typhus and maintained since 1945 in guineapigs.

Serological tests were carried out on the rabbits at intervals of 14, 16, and 27 days. In each test the sera of 24 rabbits were examined.

No significant agglutination was obtained with suspensions of *Proteus OX19*, *Pr. OX2*, *Pr. OXK*, or *Pr. XL*.

With complement-fixation tests, all the 24 sera gave negative reactions with antigens of Q fever, epidemic typhus and murine typhus. With antigens of Rocky Mountain spotted fever, 22 of the sera were positive; with boutonneuse-fever antigen, 12 were positive; and with North Queensland tick typhus antigen, 13 were positive.

These results were regarded as indicating that North Queensland tick typhus belonged to "the spotted fever group of rickettsiae". The findings are in conflict with those of PLOTZ *et al.* who reported that the reactions against Rocky Mountain and boutonneuse fever were negative. [See this *Bulletin*, 1947, v. 44, 204.]

Ten of the above rabbits were later challenged with epidemic-typhus infection, and all responded by giving positive Weil-Felix reactions and positive complement-fixation reactions against epidemic typhus antigens. Four other rabbits of the group were challenged with Rocky Mountain spotted fever infection; three of them developed positive Weil-Felix reactions, and all four gave positive fixation reactions against the homologous antigen. Five of the rabbits were challenged with boutonneuse infection; none gave a positive Weil-Felix reaction, but all gave fixation reactions against boutonneuse antigen.

The antigenic relationships of the rickettsiae were further studied by carrying out complement-fixation tests on guineapigs immunized against various kinds of rickettsiae, with the use of antigens prepared from yolk-sace cultures of the North Queensland tick typhus, by the method described by TOPPING and SHEPARD [this *Bulletin*, 1946, v. 43, 910]. The table shows the results obtained with "soluble" antigens and rickettsial suspensions; the titres observed when homologous antigens were used are shown for comparison.

Titres of Complement-Fixation Tests of Immune Guineapig Sera. Averages of 20 Tests

Antisera against	Antigens North Queensland Tick Typhus		Homologous Rickettsial Suspension
	Soluble Antigen	Rickettsial Suspension	
N. Q. Tick Typhus	248	126	126
S. African Tick Bite Fever ...	56	3	64
Boutonneuse Fever	43	10	336
Rocky Mountain Spotted Fever	103	18	240
Rickettsialpox	200	15	166
Maculatum Disease	64	0	328
Murine Typhus	0	0	512
Q. Fever (American)	0	0	416

The authors' conclusions are that the disease belongs to the "spotted fever" group of rickettsial diseases, but that the strain of rickettsia is not "synonymous" with any of the known members of the group.

John W. D. Megaw

BARTONELLOSIS

MACCHIAVELLO, A. Posible nuevo tratamiento para la bartonelosis sistemica. Auto-hemoterapia intradérmica. Mecanismo fisio-patológico de la infección bartonelar. [**Possible New Treatment of Bartonellosis. Intradermal Auto-haemotherapy.**] *Rev. Ecuatoriana de Hig. y Med. Trop.* Guayaquil. 1944, Dec., v. 1, No. 4, 341–61, 1 folding chart.

None of the methods of treatment of bartonellosis hitherto applied—liver extract, vitamins, salvarsan, compounds of arsenic and antimony, blood-transfusion, etc.—has given very good results. The author has tried what he calls "intradermal auto-haemo-vaccine therapy" and reports excellent results in 6 patients since December 1943; one a boy of 15 years, the others adults. In another, though the *Bartonella* disappeared from the blood in 6 days, death occurred 4 days later.

The following is the method adopted: 10 cc. of blood are taken into citrate from a vein at the elbow and set aside for 6 hours; then, from the deposit (avoiding the upper layer of leucocytes) is withdrawn by a syringe the amount of blood it is desired to inject—2–3 cc. intradermally and the rest intramuscularly. In a case reported in detail, after 4 weeks of "general" treatment with vitamins B_1 and C and liver extract, on the 31st day of disease the first injection was given, the second on the 35th, by which time *Bartonella* were fewer, fewer still on the 40th when a third injection was given; none were seen when later injections were given on the 46th, 55th, 62nd and 68th days of disease. In one patient the *Bartonella* organisms were not seen after 3 days;

in others in 4 days (two cases), 6 and 16 days. Vitamin administration consisted of 200–600 mgm. of vitamin C (Ascorbicin Squibb) daily intravenously, with 1 cc. of Parentosol, but the impression was that these played no specific part in the cure ; they merely improved the general condition. This treatment seemed to forestall the verrucose, eruptive stage ; at all events none of the patients so treated developed verruga.

The essential difference between this method and that of autohaemotherapy previously applied consists in the fact of *intradermal injection*, whereas others used the subcutaneous or intramuscular route—on this the author lays great stress. *H. Harold Scott*

YELLOW FEVER

Halawani, A., Abdel Aziz, A. & Ashour, M. **A Report presented to H.E. the Minister of Public Health by the Yellow Fever Mission to Nigeria (West Africa).** *J. Roy. Egyptian Med. Ass.* 1944, Aug., v. 27, No. 8, 341–90, 4 figs. & 2 maps. [29 refs.] [Recd. 13 Dec., 1948.]

Paoliello, A. Contrôle da febre amarela e de outras doenças transmitidas por mosquito. [**Control of Yellow Fever and other Mosquito-borne Diseases.**] *Bol. Oficina Sanitaria Panamericana.* 1948, Nov., v. 27, No. 11, 1005–44, 2 maps. [89 refs.] English summary.

This is a summary of some methods of control of the mosquito-borne diseases, yellow fever, malaria, filariasis and dengue. The great part of the article deals with the use of DDT against mosquitoes and of virus as a prophylactic against yellow fever and the use of the viscerotome in diagnosis.

DDT is an efficient insecticide, but it has its limitations. House-spraying, for example, will not eliminate *Aëdes aegypti* whose eggs are viable for a period longer than the spray is effectual. It must also be used as a larvicide in domestic water-containers. There is need also to search for obscure or hidden foci and destruction of adult insects. DDT must be used also in vessels sailing to and from mosquito-infected ports. In the prophylaxis of yellow fever, the virus 17D vaccine, long in use, is compared with a neurotropic French strain ; it is shown that the former is not easy to preserve and the conclusion is reached that the French strain is better.

Visc-rotomy specimens of liver obtained from males between 10 and 50 years of age who die in less than 11 days from the onset of a fever will reveal all that is necessary as regards silent areas of jungle yellow fever. Studies in Colombia showed that of 352 cases of yellow fever discovered by viscerotomy, 92 per cent. were males and 81 per cent. were persons between 10 and 50 years of age.

Anti-*aegypti* measures will be effective against dengue as against yellow fever.

In malaria control, DDT is still the basic element, with drug treatment secondary. DDT has also done much to solve the problem of filariasis control but a good second is Hetrazan (methyl diethyl-carbamil piperazine hydrochloride) in attacking the filarial embryos. *H. Harold Scott*

RABIES

REMLINGER & BAILLY, J. Sur les échecs du traitement antirabique. [**On the Failures of Anti-Rabies Treatment.**] *Bull. Acad. Nat. Méd.* 1948, v. 132, Nos. 35/36, 598–9.

After trauma or emotional disturbance, rabies often makes an unexpected appearance in human beings as well as in lower animals, some time after a full course of anti-rabies injections has been regularly administered. In explanation of such occurrence the authors advance an interesting hypothesis which, in the article under review, is considered along the lines summarized below :

When the rabies virus, now regarded as a nucleoprotein, reaches a neurone, its action is to interfere with the anabolism of the cytoplasm. Inasmuch as the neurone itself elaborates the substance of the rabies virus which parasites it, such interference results in the continued production of new molecules of rabic nucleoprotein, which are conveyed *via* axis cylinders, their prolongations and synopses to healthy neurones, wherein the process is repeated. The effect of this chain reaction is the rapid invasion of all the chief elements of the nervous system, and so rabies occurs.

Such, however, is not always the sequence of events. Neurones can, in certain circumstances as yet imperfectly understood, defend themselves against attack by the virus. The mechanism of defence is that of all living cells against a foreign protein—a precipitation of the latter in an insoluble state, *i.e.* flocculation. Under the influence of this defence reaction, therefore, the molecules of rabies virus may, on reaching the neurones, pass from their ordinary colloidal state to a state of flocculation—the first step towards total destruction of the virus which, both under natural and experimental conditions, frequently takes place. This phenomenon is termed by LEVADITI "*neuro-infections auto-stérilisées*".

It follows, then, that the rabic nucleoprotein, once flocculated in the neurones, no longer provokes any cellular reaction ; the production of fresh virulent molecules is arrested and no disturbance of function ensues.

Flocculation is, however, a state of equilibrium, essentially unstable and reversible ; if, then, by any action, mechanical, chemical or electrical, this equilibrium is upset, the state of flocculation passes immediately to one of dispersion, *i.e.* to the colloidal state. Resulting from this change of state, the rabic molecules rapidly recover their original properties and, as soon as a sufficient number of neurones has been affected, the disease abruptly manifests itself.

In the light of this new hypothesis, the effect of anti-rabies treatment may now be examined. Specific treatment consists in the inoculation of suspensions containing partially virulent or wholly avirulent rabic protein. After a sufficient number of injections, the body fluids acquire viricidal properties, evidenced by the fact that the blood serum becomes capable of neutralizing the rabies virus *in vitro*. As soon as ever this stage is reached, the virulent molecules of rabic nucleoprotein, which have invaded the neurones, flocculate and such flocculation, in the vast majority of cases, is followed by a disappearance of the infective nucleoprotein.

In a minority of cases, however, in consequence of undue excitation or inhibition of the neuro-vegetative system (*e.g.* fear, anger, shock) or in consequence of an upset in the acid base equilibrium of the blood and tissues (*e.g.* fatigue, overwork, violent muscular effort), there may occur, even after a full course of anti-rabies treatment, a reversion, on the part of the rabic molecules, from

the state of flocculation to the colloidal state—a reversion which accounts for the unexpected onset of the disease and for certain failures of anti-rabies treatment. *G. Stuart*

Mace, D. L. **Five Unusual Cases of Canine Rabies.** *J. Amer. Vet. Med. Ass.* 1949, Jan., v. 114, No. 862, 30–32.

PLAGUE

Hérivaux, A. & Toumanoff, C. Étude de la " faune pulicidienne domiciliaire " des rats au cours d'une épidémie de peste à Saïgon ; ses conséquences pratiques. [**Practical Significance of the Results of Studying the " Domestic Flea Index " in Rats during a Plague Epidemic in Saigon.**] *Bull. Soc. Path. Exot.* 1948, v. 41, Nos. 5/6, 318–25.

From June, 1943, to May, 1944, the authors made regular collections of fleas from the floors of human habitations in Saigon. They considered that from such a flea survey they could obtain information of value in the study of plague transmission.

The fleas they were concerned with were those which had left the rats and were to be found in the dust on the floors of the houses. They record their monthly totals in three tables. One lists the numbers of fleas caught in huts with earth floors ; the second those found in stone houses with tiled floors and the third table combines both sets of data. The number of premises is not given.

Of 6,820 fleas collected throughout the year, only 12 were *Pulex irritans*. *Ctenocephalides canis* and *C. felis* were most numerous (6,465) and fleas of the genus *Xenopsylla* (*cheopis* 200 and *astia* 133) less so, but these latter species were more common than *Ctenocephalides* in June and July, during a plague epidemic. *X. cheopis* is the main vector, though *X. astia* is also important ; the former being more common than *X. astia* on the floors of the stone houses, while in the huts with beaten earth floors there were more *X. astia* than *X. cheopis*.

Figures are also given to show that numbers of these fleas contained human blood.

As a result of this survey, the authors are convinced that, in Saigon at least, a flea index, calculated from such a survey of fleas caught from among the floor dust of human dwellings, is of more value in assessing the risks of plague transmission than is the usually accepted " *cheopis* index ". *H. S. Leeson*

Favarel, R. Le rôle du pou de l'homme dans la transmission de la peste à Madagascar. [**The Rôle of the Human Louse in the Transmission of Plague in Madagascar.**] *Bull. Soc. Path. Exot.* 1948, v. 41, Nos. 9/10, 576–80.

The author was unable to find evidence of a significant difference between the virulence of a culture of plague bacilli obtained from the bodies of three lice, the dead body of a child who had died of plague, and of another culture obtained by spleen puncture of the child.

A study of the epidemiological conditions prevailing in Madagascar yielded no evidence to support the view that the human louse had played an appreciable rôle in the transmission of plague from man to man. *John W. D. Megaw*

WAGLE, P. M. & BEDARKAR, M. K. **Pneumonic Plague and its Treatment.** *Indian Med. Gaz.* 1948, Sept., v. 83, No. 9, 406–8.

Six cases of pneumonic plague were treated by streptomycin given by the intramuscular route. The usual dosage was 0·66 gm. every four hours till clinical improvement was observed, when the dose was diminished. The total amount given ranged from 15·3 to 38·0 gm.

Five of the six patients recovered; the fatal case was one of secondary pneumonic plague, and death occurred on the second day. Two of the patients who recovered had secondary pneumonic plague, the other three had primary attacks. Three of the cured patients received antiplague serum, the usual dose was 40 cc. twice daily. The other two patients who recovered were also given serum and in addition they received sulphamerazine, 7·0 to 9·0 gm. in divided doses on the first day; then 3·0 to 4·0 gm. daily.

The authors attribute the recovery of the five patients to streptomycin, but they advise the use of serum in addition, with or without sulphamerazine. It is stated that primary plague pneumonia is often of the lobar type, sometimes with "stringy" sputum, sometimes with little or no sputum. Leocopenia is usual; in the early stage blood cultures are negative. *John W. D. Megaw*

CHEN, T. H. **A Preliminary Report of Rat-Poison with Red Squill, "1080" and Antu.** *Chinese Med. J.* Shanghai. 1948, July, v. 66, No. 7, 384–6.

"1. Red squill, when used in a concentration of 10 per cent. in baits containing animal fat, gave results comparing favorably with those obtained with barium carbonate.

"2. '1080' proved, as in the United States, so also in China, a most efficient rat-poison, but it must be handled and used by specially trained workers only.

"3. ANTU was found in Foochow to be almost as effective against *R. rattus* as against *R. norvegicus*. Prospects for utilizing it for universal rat-poisoning campaigns in China are therefore good and since ANTU acts by contact, its application could be rendered fairly safe."

CHOLERA

OMAR, W. & VASSILIADIS, P. C. **Study of the Vibrios isolated at El-Tor Quarantine Camp during the Pilgrimages of 1941–42 and 1942–43.** *J. Roy. Egyptian Med. Ass.* 1943, Oct., v. 26, No. 10, 348–56.
[Recd. 13 Dec., 1948.]

"1. During the pilgrimage of 1941–42, vibrios were found in 2·28 per cent. of the stools examined, while in only 0·56 per cent. were they found in the 1942–43 pilgrimage. As during this last pilgrimage, there were no Indian pilgrims at the Hedjaz, this might probably explain the smaller percentage of vibrios found in this year.

"2. Agglutinins were found, in the sera of carriers of non-agglutinable vibrios, against some of these vibrios, especially against one particular vibrio (*i.e.* N.22) which was agglutinated by its carrier serum in 1/800. It is assumed that these agglutinins represent normal antibodies.

"3. Some characters of the non-agglutinable vibrios isolated from the 1941–42 and 1942–43 pilgrimages are described. It is of interest to note that while in both groups the majority of these vibrios belonged to fermentation

group I of Heiberg, all the other vibrios of the first year belonged to group V, whilst all the rest of the second pilgrimage belonged to group III except one that belonged to group II."

FELSENFELD, O. **Antigenic Relationship of *Salmonellae* to Inaba Strains of *Vibrio comma* isolated in Egypt.** *Proc. Soc. Exper. Biol. & Med.* 1948, Oct., v. 69, No. 1, 95–6.

GOHAR and MAKKAWI found that strains of the cholera vibrio from the recent outbreak in Egypt were agglutinated by *Salm. enteriditis* sera [this *Bulletin*, 1948, v. 45, 706]. The present author tested 3 strains of the vibrio (Inaba type) obtained from the Egyptian epidemic against 25 O, 2 Vi and 39H *Salmonella* sera. Live antigens were used and the preparation of antisera and the technique of agglutination and absorption tests were carried out according to standard methods, which are quoted.

The results are shown in detail in three tables, which show that agglutination occurred with dilutions of various *Salmonella* sera as high as 5 to 25 per cent. of their titre against the homologous *Salmonella* when the serum contained agglutinins for the *Salmonella* antigenic factors I, XII or g. Absorption tests confirmed that parts of these three antigens were present in the strains of cholera vibrio. Sera prepared against the latter also agglutinated *Salmonella* strains containing the three antigenic factors quoted. The author therefore shows that the three Inaba strains ("K", "4" and "8") of the cholera vibrio isolated recently in Egypt harboured fractions of *Salmonella* I, XII and g antigens. *H. J. O'D. Burke-Gaffney*

TAO, S. C., WOO, M. O. & LOH, W. P. **Clinical Observations on 687 Cases of Cholera.** *Chinese Med. J.* Shanghai. 1948, July, v. 66, No. 7, 377–84.

The findings in 687 cases of cholera in Shanghai, in which the diagnosis was confirmed by the isolation of the vibrio, are examined and tabulated. The majority of the patients were poorly educated labourers and vagabonds and their families. Incidence was at all ages from 3 to 77 years and highest in the 21–30 age group. There was a preponderance in males over females of 5 : 3. The disease occurred in 8·3 per cent. of those whose inoculation history could be ascertained.

The figures given for the percentage of cases showing different symptoms are in accordance with usual experience. Uraemia was the most serious complication and occurred in 27 patients (3·9 per cent.) of whom 8 died, giving a mortality rate of about 30 per cent.

In discussing uraemia, developing after the acute stage with retention of non-protein nitrogen, it is considered that haemorrhages in the cortex and damage to the tubules result from the effect of prolonged or severe circulatory disturbance, restoration of efficient renal function being delayed or failing to occur even after dehydration and collapse have been corrected. It was noted that many uraemic patients "developed generalised oedema of mild to moderate degree when slight excess of saline was pushed parenterally in an attempt to promote urinary excretion".

In uncomplicated cases the average duration of illness was 4 to 5 days and with uraemia 7 to 8 days. Treatment was by intravenous transfusion of normal saline and with 0·5 per cent. sodium bicarbonate in half-normal saline. Glucose saline was given in cases of relatively prolonged course or when there was uraemia and acidosis. At a period when the saline solution used was known not to be pyrogen-free the majority of patients had febrile reactions after transfusion. When pyrogen-free saline was used, mild or moderate fever occurred in only 31·5 per cent. of cases.

The case mortality rates experienced in India and China at periods when different methods of treatment were used are shown in a table for comparison. From a figure of 59 per cent. (in Calcutta in 1895–1905) there has been a striking drop in the death rate following the introducing of treatment by saline transfusion, and experience of the use of the method. In the present series of bacteriologically confirmed cases in Shanghai the rate was 4·7 per cent. and including cases diagnosed clinically the figure was 6·2 per cent. The highest mortality rate was in the age group 0–10 years (17·9 per cent.).

No statistical interpretation can be placed on the results of a short series of 41 cases treated with 1 gramme of sulphadiazine orally every 4 hours for 4 or 5 days along with an equal amount of sodium bicarbonate. A general impression was gained that the treatment reduced the severity and duration of the attack. The authors are highly sceptical of the likelihood of any striking effect being obtained by chemotherapeutic treatment in cholera in view of the nature of the disease, in which the primary requirement is the replacement of fluid.

In a daily bacteriological examination of the stools of 218 cases, until two successive negative cultures were obtained, it was found that 90 per cent. were negative on or before the 6th day : none of the cases was positive beyond the 8th day. *J. Taylor*

SINGER, E., WEI, S. H. & HOA, S. H. **Cholera Immunization**. *J. Immunology*. 1948, Oct., v. 60, No. 2, 181–7.

The response to immunization with cholera vaccine prepared in different ways was tested in human subjects. An Ogawa strain isolated in Nanking was used for the preparation of the vaccine, suspensions of the growth on beef extract agar being first prepared by washing off with physiological saline solution. The suspensions were treated in the following ways :—

1. Heating at 55° to 56°C. for 30 minutes and preserving with 0·5 per cent. phenol.
2. Adding 0·3 per cent. formalin to kill the vibrios and preserving with 0·5 per cent. phenol.
3. Immersing the containers in boiling water and maintaining the temperature at 100°C. for 30 minutes, 0·5 per cent. phenol being subsequently added.
4. Adding absolute alcohol to a concentration of 75 per cent. and then diluting to the required vibrio content (8,000 million per ml.) with alcohol adjusted to 20 per cent.

[Vaccine of the type very commonly used, in which the only treatment employed is the addition of phenol, was not tested.]

The experimental subjects were given subcutaneous injections of 4,000 million, 4,000 million and 8,000 million organisms at intervals of 7 days. The reactions to inoculation were insignificant and did not vary appreciably with any of the types of vaccine used.

In a first series of subjects no significant difference was found in the agglutination titres of those given either the vaccine heated at 56°C. or the vaccine treated with formalin or alcohol. Vaccine heated at 100°C. appeared to give a better antibody response, but in a second series in which the vaccines heated at 56°C. and 100°C. were compared this difference did not occur. A chance variation or some extraneous factor may have been responsible for the first finding.

The effect of intracutaneous inoculation of vaccines heated at 56°C. and 100°C. was also tested. Immunization with two intracutaneous injections (0·1 ml. followed by 0·2 ml.) gave an antibody response that did not differ significantly from that of the groups vaccinated by the subcutaneous route with

the larger doses. When three intracutaneous doses of 0·2 ml. were employed the agglutination response obtained was higher than by any other method. In some instances, however, a small abscess formed about 4 to 6 days after the third injection. "Although those abscesses were quite insignificant and their formation was not accompanied by any marked discomfort they must be considered as an undesirable complication and, at present, a contraindication against the use of intracutaneous vaccination in cholera prophylaxis."

In a previous communication [this *Bulletin*, 1949, v. 46, 37] the authors had described the effect of filtrates of cultures of *V. cholerae* in causing shedding of the epithelium of the ileum of the guineapig and the neutralization of that effect by rabbit serum containing antibodies against the somatic antigen of the vibrio. The same effect was obtained with the sera of immunized human subjects during the course of this study. The neutralizing antibodies were removed by absorption with a boiled suspension of *V. cholerae*.

The antibodies produced by the vaccines prepared in different ways were shown to be identical by cross absorption tests. *J. Taylor*

AMOEBIASIS AND INTESTINAL PROTOZOAL INFECTIONS

DE FIGUEIREDA, J. M. P. A carência alimentar e a parasitose intestinal (anquilostomiase e amebiase) no determinismo da úlcera duodenal. (Contribuição para o estudo de patologia regional.) [**Avitaminosis and Intestinal Parasitism in the Aetiology of Duodenal Ulcer.**] *Bol. Geral. de Med.* Nova Goa. 1947, Jan.–Dec., Ser. 29, Nos. 1/12, 27–42.

The author puts forward the view, and gives notes of nine cases in support of his thesis, that food deficiencies associated with amoebiasis or ankylostomiasis have some aetiological connexion or play a part in the causation of duodenitis and duodenal ulcer. The author bases his statements on experience of several years' observation [but it is not clear, and it would be difficult to demonstrate, that the conditions are aetiologically connected and not merely chance concomitants]. *H. Harold Scott*

RICKARDS, A. G. **On the Incidence of Protozoal and Bacillary Intestinal Infections in Men of the Royal Air Force returning from Service in Tropical and Subtropical Lands.** *J. Trop. Med. & Hyg.* 1949, Jan., v. 52, No. 1, 2–11. [38 refs.]

The purpose of this paper is to record the results of certain investigations undertaken in the examination of R.A.F. officers and men immediately prior to their demobilization. All were examined immediately after disembarkation from overseas. The subject is discussed under three main headings, namely: the post clinical histories of diarrhoea and dysentery; the incidence of various protozoal organisms and their relationship to previous clinical history in a similar group; and the pathogenesis of *Entamoeba histolytica*. In the delineation of the geographical area two broad distinctions were made, namely: Indian and Mediterranean theatres. The questionaries from 22,200 men were examined, representing an unselected sample. For simplicity's sake, all cases of dysentery or severe diarrhoea that were not protozoal, were classified under the heading of "bacillary dysentery". The principal value of the figures obtained is to be found in their comparison rather than in their absolute totals. All faeces examinations were carried out by the author so accordingly the personal error has been kept more or less constant. In 2,000 cases, some 2,500

specimens were examined and all in which *E. histolytica* was suspected or diagnosed on the initial preparation were re-examined in a freshly-voided specimen. It was possible to examine one specimen only and therefore an adjustment has to be made so that the true incidence is about three to five times that established by a single examination [see this *Bulletin*, 1935, v. 32, 220]. Calculation in this fashion would give the true incidence of *E. histolytica* as follows :—

Mediterranean group, 10·41 to 17·35 per cent.
India group, 21·99 to 36·65 per cent.
and the incidence of non-pathogenic protozoa as

	India group	Mediterranean group
Entamoeba coli	15·1	18·1
Endolimax nana	10·00	7·5
Iodamoeba bütschlii	3·8	3·05
Giardia lamblia	2·9	2·15

The incidence of amoebic dysentery was nearly seven times as high among those returning from the Indian area (1·76 per cent. against 0·26 per cent.). On the results obtained from this survey it can be estimated that about half a million men might be expected to return from overseas harbouring *E. histolytica*. The incidence of *E. histolytica* has not been found to vary between two groups of men composed of those who had suffered from bacillary dysentery and those who had not. The variation in the incidence of the parasite is not significant between those giving a past history of dysentery, and those who had been free from it, but that of *E. histolytica* is significantly higher in those presenting a past history of amoebic dysentery. It is suggested that the strain of *E. histolytica* which affected men in the Indian theatre is of greater virulence than that endemic in the Mediterranean.

The clinical histories of 25 symptomless cyst-passers were followed up for periods of 6–10 months and showed that three of the men developed symptoms of gastro-intestinal dysfunction probably related to the parasitic infection.

P. Manson-Bahr

Bertrand-Fontaine, Mme., Fauvert, R. & Schneider, J. Trois observations d'abcès aigus amibiens du foie. [**Three Cases of Amoebic Abscess of the Liver seen in Paris.**] *Bull. et Mém. Soc. Méd. Hôpit. de Paris.* 1948, Nos. 30/31, 1079–83, 1 fig.

During the past year the authors, in Paris, have discovered three cases of abscess of the liver in patients who have never been out of the metropolis. In one. active forms of *E. histolytica* were demonstrated in the liver pus and cysts were found in the faeces. *P. Manson-Bahr*

Blas Ruiz, H., Gruhn, E. & Schouten, G. Primer caso de absceso hepático por entameba disentérica, observado en el Paraguay. [**First Case of Amoebic Abscess of the Liver recorded in Paraguay.**] *An. Facul. de Ciencias Med.* Asuncion, Paraguay. 1946, June, v. 6, No. 23, 247–55, 5 figs.

The following is a translation of the authors' summary :—

The authors describe the first case of liver abscess caused by dysenteric amoebae in Paraguay. The patient was a Netherlands priest who had probably contracted the disease in Turkestan 20 years previously. Operation in Paraguay

in February 1942, together with previous radiological examination, revealed the presence of a right hepatic abscess which had extended into the thorax. Microscopic examination showed entamoebae resembling those described by Councilman and Lafleur. Treatment consisted of emetine injections and tablets of yatren and stovarsol. The patient was discharged cured within three months. *H. J. O'D. Burke-Gaffney*

El Kordy, M. I. **On the Cultivation of *Entamoeba histolytica* in Hydatid Fluid.** *J. Roy. Egyptian Med. Ass.* 1944, Aug., v. 27, No. 8, 329–40. [20 refs.] [Recd. 13 Dec., 1948.]

Erdei, A. **Pulmonary Tuberculosis complicated by Amoebic Hepatitis.** [Memoranda.] *Brit. Med. J.* 1949, Jan. 1, 18.

A woman of 36, who had had pulmonary tuberculosis for some 10 years, had been complaining for 8 of those years of dragging pains in the right iliac fossa, and more recently, in the right epigastric region. The pains were independent of food, worse on standing and were increasing in frequency. The bowels were regular and the stools macroscopically normal. The patient had had three or four attacks of diarrhoea, lasting a few days each, between 1939 and 1944; it appears that blood and mucus were passed on two occasions. The patient had never been in tropical countries, but had been on trips to Paris, the south of France and the Dalmatian coast before the war.

The caecum proved to be ballooned, doughy and tender. A small area of tenderness was detected in the right lobe of the liver, about 2·5 cm. to the right of the xiphoid process, and was most pronounced in the intercostal space above. On screening, the right diaphragm was slightly elevated, with diminished movement. On sigmoidoscopy, the rectal mucosa proved to be congested and oedematous, with several submucous haemorrhages and a few small healed ulcers at 10 cm.

There was some hypochromic anaemia, leucocytes were 3,600 per cmm. with normal distribution. Among the laboratory tests it is noted that the nicotinic acid tolerance was 450 mgm. Examination of the stools revealed two typical cysts of *Entamoeba histolytica* in the sixth specimen.

The patient was treated with 10 injections of emetine, together with penicillin, and diodoquin and consecutive emetine bismuth iodide and carbarson were given. The liver became very tender after the second emetine injection, but the tenderness disappeared after the sixth.

More attacks of diarrhoea occurred after the improvement from the specific treatment. Later examination revealed the presence of *Giardia intestinalis* in the stools and of *Shigella flexneri* in a sigmoidoscopy swab (but not in the stools). The patient recovered after treatment by sulphasuxidine and her motions do not now exceed two daily.

The author points out that abdominal tuberculosis figured too prominently in the differential diagnosis and stresses the need for keeping chronic amoebiasis in mind when dealing with obscure conditions. He also points to the value of a rapid liver-function test, such as that of nicotinic acid tolerance.

H. J. O'D. Burke-Gaffney

Verner, H. D. **Pulmonary Amebiasis due to Hematogenous Spread. Report of a Case.** *Bull. Charlotte Memorial Hosp.* Charlotte, N. Carolina. 1948, Dec., v. 3, No. 1, 3–6.

This paper records the rather curious story of a 55-year-old farmer whose symptoms were directed to his general condition rather than to the digestive tract. These consisted of generalized abdominal pain, a productive cough and

fever. There were occasional attacks of diarrhoea with occasional tarry-black stools. During this time he was treated, at intervals, with emetine without obvious improvement. On admission to hospital, attention was directed to the physical signs at the base of the left lung where, on X-ray examination, a non-homogeneous ill-defined consolidation was revealed, while subsequent instillation of lipiodol showed the appearance of bronchiectasis. Consequently a left lower lobectomy was performed. No specific diagnosis was made, but bronchiectasis was not confirmed. Further X-ray films showed consistently a small amount of fluid at the left costo-phrenic angle. One month later a posterior thoracotomy was done and the purulent fluid was drained. The patient was discharged apparently well. Two weeks later he became acutely ill with cough and respiratory signs necessitating a repeated thoracotomy. Subsequently a raised fluctuating swelling appeared in the right upper abdominal quadrant which, on incision, yielded a large amount of thick, creamy pus. From this time onwards he gradually developed septicaemia and eventually died.

At autopsy a typical amoebic ulcerative colitis was revealed extending from the caecum to the descending colon and in the liver there were two large abscesses in the right lobe, together with thrombophlebitis of a large radicle of the hepatic vein. This radicle emanated from one of the abscesses and contained a firmly adherent thrombus which extended into the vena cava at the junction with the hepatic vein. Histologic sections revealed the presence of numerous *E. histolytica* in the margins of the intestinal ulcers and in the wall of the liver abscesses; renewed search of the sections of the lung, obtained by previous lobectomy, also revealed numerous amoebae in the lung tissues.

Two factors were responsible for failure to recognize the true condition in the first instance. In the first place, repeatedly negative laboratory examinations of sputum and faeces tended to discourage the diagnosis of amoebiasis and in the second it was difficult to reconcile the position of the lung abscesses on the assumption of amoebiasis.

It is claimed that this case illustrates the mechanism of septicaemia. If the organisms travel through the portal system, producing a liver abscess, the latter may give rise to a thrombophlebitis of the hepatic vein, thus creating a secondary focus of dissemination. It is assumed that the liver abscess, which was not clinically evident, antedated the pulmonary abscess.

P. Manson-Bahr

DE SALVE, A. Sopra un caso di amebiasi a sintomatologia setticemica. [**A Case of Amoebiasis with Septicaemic Manifestations.**] *Boll. Sanitario d. Tripolitania.* 1948, Jan.–June, v. 6, Nos. 1/2, 4–7.

The English summary appended to the paper is as follows :—

" The author describes a case of amoebiasis which, because of its symptomatology, is defined as a case of amoebiasis with unusual septic characteristics.

" After having discussed the case from the clinical point of view, he gives the pathogenic interpretation of it by postulating that Entamoeba histolytica can produce, besides the known cytolysin, also a substance capable of toxic action and responsible for the peculiar symptomatology shown by the patient."

DO PRADO, Felicio C. Simulação da colecistite crónica pela amebiase intestinal. [**Intestinal Amoebiasis simulating Chronic Cholecystitis.**] *Hospital.* Rio de Janeiro. 1948, Oct., v. 34, No. 4, 489–93.

The English summary appended to the paper is as follows :—

" In 500 cases of intestinal amebiasis the author found 11 cases in which there was a prevalence of symptoms generally attributed to affections of the biliary

ducts, thus suggesting the clinical hypothesis of cholecystitis. The patients showed steady or intermittent pain in the hepatic region, tenderness over the vesicular area, nausea before breakfast, and certain dyspeptic-pain symptoms caused by foods, especially fatty foods. Cholecystography and duodenal intubation did not reveal any abnormality in these patients ; feces examination was positive for *Endamoeba histolytica* and the apparently vesicular symptoms disappeared with the specific antiamebic treatment. Such cases are explained by the author to be due to general toxic manifestations acting sporadically upon the vesicular functions, and perhaps, in some cases to a colitis predominating on the hepatic flexure.

" In view of the relative frequency of intestinal amebiasis the author calls attention to the fact that this organic colonopathy should be mentioned, at the side of the functional, in differential diagnosis of chronic cholecystitis."

Clerc, S. & Bergeret, C. Quelques observations d'aspects chirurgicaux de l'amibiase intestinale. [**Some Notes on the Surgical Aspects of Intestinal Amoebiasis.**] *Bull. Méd. de l'Afrique Occidentale Française.* 1947, v. 4, No. 4, 415–20.

This short paper consists of brief clinical notes on the cases of eight patients. In three cases abscesses in the right iliac fossa were incised and amoeba were subsequently found in the pus in two of them ; in one patient, who was found at necropsy to have multiple liver abscess with amoebae in the pus, perforation of the caecum led to fatal peritonitis ; in one patient the diagnosis was made during operation for supposed appendicitis, by the appearance of the caecum which was oedematous and covered by a veil of loose adhesions, whilst the appendix appeared to be normal. The remaining three patients had masses in the left iliac fossa due to perisigmoiditis ; two of these suppurated and needed incision, but no amoebae were found in the pus, whilst the third resolved under emetine treatment. All three patients had symptoms of subacute intestinal obstruction and radiological examination after barium enema showed this to be due to pressure on the colon ; emetine treatment brought about rapid improvement and confirmed the diagnosis. The demonstration of amoebae in the granulations forming after incision of an abscess in two cases is so rare that the authors have included a short abstract of a paper on this subject by Touraine and Duperpat, in which cutaneous amoebiasis is divided clinically into (1) infection by extension (*a*) following incision of an abscess, (*b*) perianal ; (2) by inoculation (*a*) cutaneous, (*b*) genital ; (3) allergic dermatoses in patients suffering from amoebic dysentery. Amoebae are found in the stools in 35 per cent. of these patients.

W. L. Harnett

Lavier, G., Crosnier, R. & Merle, F. Le traitement de l'amibiase par la conessine. [**The Treatment of Amoebiasis with Conessine.**] *Bull. Soc. Path. Exot.* 1948, v. 41, Nos. 7/8, 548–53.

A preliminary report [this *Bulletin*, 1948, v. 45, 1086] has already appeared from this source on the use of extracts of *Holarrhena africana* [*floribunda*] in the treatment of amoebiasis. This followed the demonstration by Durieux *et al.* [*ibid.*, 905] of the therapeutic activity of conessine in amoebiasis.

Forty-two cases of acute amoebiasis constitute the material for the present report, of which 40 were repatriates to France from the Far East, and 2 from North Africa. With the exception of 3, all these patients had previously been treated with emetine on 3 to 6 occasions. Emetine resistance is common among those repatriated from the Far East ; it is either a partial or complete " true " resistance to the drug, or a " pseudo-resistance " which is amenable to treatment.

Both the hydrochloride (33 cases), and the hydrobromide (6 cases) [? 9] salts of conessine were used. The drugs were given orally; initially the dose was 0·5 gm. daily; this was reduced to 0·4 gm. or 0·3 gm. daily if intolerance was manifested. The gross dosages ranged from 3·5 gm. to 6·8 gm.; usually 5·0 gm. were given over a period of two weeks. There was no evidence of "true" toxicity of the compounds; the side-effects chiefly encountered were tremors of a Parkinsonian type (13 cases), and insomnia, nightmares and disturbances of sleep (20 cases). There was improvement in the general health in all cases under treatment; and the stools rapidly were restored to normal. Rectoscopic examinations showed the mucosa to have healed completely (13 cases), or substantially (12 cases), after the conessine course.

Seven of 10 cases on re-examination 6 weeks after the conclusion of treatment had no parasites in the stools [number examined unspecified]. Of the other three patients, one was passing loose stools containing amoebae; the remaining two were passing cysts. All these three were again rapidly "sterilized" by retreatment with conessine. As conessine is not invariably successful in eradicating an *E. histolytica* infection, it should be followed by further therapy to forestall relapse; suggestions are made as to the nature of this after-treatment.

[The words "cure" and "sterilization" are used in this paper for "clinical cure" and "temporary absence of parasites from the stools", respectively. The claims that the results of conessine treatment are "brilliant", and that the drug is superior to emetine in the treatment of amoebiasis do not appear to the reviewer to be substantiated by the evidence presented.]

A. R. D. Adams

Chou, T. C. & Jang, C. S. **Chemotherapeutic Studies on Ya Tan Tze. 2. Ya Tan Tze** (*Brucea javanica*) **on Experimental Amebiasis.** *Chinese Med. J.* Shanghai. 1948, July, v. 66, No. 7, 359–63. [14 refs.]

"Ya Tan Tze, the seed of Brucea javanica, and its crystalline principles, substances *A*, *B*, and *C*, have been tested for their therapeutic value on experimental amebiasis in dogs. The whole kernel of the drug is highly effective in eliminating the parasite, but the survival periods of the treated animals are not prolonged. The substance *B*, a phenolic compound, acts like the crude drug and may, therefore, represent its active principle. In the doses used, both the crude drug and the substance *B* produce vomiting and diarrhoea and other signs of gastro-intestinal irritation. The other two principles, *A* (an organic acid) and *C* (a glycoside) have been tried on one case each, and the results are, therefore, inconclusive."

Smyly, H. J. **A Note on the Treatment of Amoebic Infection with** *Brucea javanica* **Seeds.** *Chinese Med. J.* Shanghai. 1948, July, v. 66, No. 7, 363–5.

A cold aqueous extract of *Brucea javanica* seeds was found to be highly amoebicidal *in vitro*; hot aqueous extracts were feebly so; and alcoholic extracts were not amoebicidal [for earlier work on this plant, see this *Bulletin*, 1937, v. 34, 955].

Twenty-eight Cheeloo University Hospital employees found to be passing *E. histolytica* cysts were treated orally, thrice daily for ten days, with 0·1 gramme pulverized decorticated seeds of *B. javanica*. Nearly half of these persons suffered from nausea and vomiting while on the drug, one so severely that the treatment had to be stopped; a few had dizziness or mild diarrhoea; six individuals suffered no side effects at all. Two months later the stools of 25 of these patients were re-examined, and 17 of them found still to be passing cysts.

Seventeen patients with acute amoebic dysentery were similarly treated by the oral route, either *ab initio* or after a few preliminary injections of emetine ; improvement followed in every case, and 2 patients appeared to be sterilized of their infections four weeks after conclusion of treatment, while 10 showed no *E. histolytica* at the end of treatment. *A. R. D. Adams*

Deschiens, R., Lamy, L. & Marchal, G., Mlle. Sur un flagellé indéterminé isolé des selles d'un français revenant de Guinée. [**An Unidentified Flagellate isolated from the Stools of a Frenchman returned from Guinea.**] *Bull. Soc. Path. Exot.* 1947, v. 40, Nos. 11/12, 435–9, 4 figs.

In the stools of a Frenchman returned from Guinea, the authors found *Dientamoeba fragilis*, *Entamoeba histolytica* and a flagellate at first identified as *Trichomonas hominis*. They isolated and maintained cultures of an amoeba and the flagellate ; however, at the end of a month they lost the amoeba, but the flagellate culture was maintained for over three months, by means of numerous subcultures. The medium they used was coagulated horse serum, Ringers' solution, rice starch and " 1·162F " [no indication of the composition of this is given] in a concentration of 1 in 1,000, with periodic transfers to whole egg with the same medium (containing 1·162F) added.

It was soon realized that the flagellate was not a *Trichomonas*. It was round, 7μ in diameter, with three flagella and no undulating membrane ; it had a large nucleus with a large central karyosome, in a single mass at the periphery of the cytoplasm. The characteristic feature was a large club-shaped appendage, 4μ in length, that protruded from the body of the flagellate.

Grassi and other authors have described a flagellate, *Joenia annectens*, in termites with a similar pseudopodic protusion, but this parasite differs from *Joenia* in other respects. The authors consider that it has the characters of an *Enteromonas*, but of a species not previously described. They have named it *Enteromonas hervei* n. sp., pending further study to decide if it constitutes a new genus. *L. E. Napier*

RELAPSING FEVER AND OTHER SPIROCHAETOSES

Vigors Earle, G. K. La fiebre recurrente. [**Relapsing Fever.**] *Rev. Ecuatoriana de Hig. y Med. Trop.* Guayaquil. 1944, Dec., v. 1, No. 4, 362–72, 1 fig., 1 chart & 1 map. [24 refs.]

The English summary appended to the paper is as follows :—

" 1. Three cases of relapsing fever, diagnosed by the discovery of *B. recurrentis* in the blood examination, are described.

" 2. All of the cases acquired their infection in the Province of Esmeraldas.

" 3. The localities within the province and adjacent Colombian territory where infection is most likely to occur are indicated.

" 4. An account of the occurrence of the disease in adjacent Colombian territory is given.

" 5. The heightened susceptibility of Europeans, white Americans and non-resident Ecuadoreans to the disease is pointed out ; the relative immunity of the local negro population is observed.

" 6. The probable role of *Ornithodoros venezuelensis*, described by Leon, as a transmitting agent from animal to man, is commented upon.

" 7. Animal reservoirs (mammals) are listed.

" 8. Some aspects of treatment with arsenicals and penicillin are considered."

LEPROSY

HAMERS, S. L. T. M. & HERMANS, E. H. Enkele waarnemingen bij leprapatiënten in Nederland. [**Some Observations on Leprosy Patients in the Netherlands.**] *Nederl. Tijdschr. v. Geneesk.* 1948, Oct. 23, v. 92 (iv), No. 43, 3409–19, 6 figs. on 3 pls. English summary.

In a rather discursive paper some data are given upon 40 new leprosy patients segregated in the leprosy centre in Holland. There appears to be no evidence that the infection was contracted in the former Japanese prison camps in the Dutch East Indies. The earliest symptoms were occasionally directed to the nose, more commonly to fatiguability, but most frequently there was an eruption, symptoms of nervous irritability or nerve injury. The Mitsuda reaction gave accurate information upon prognosis, whilst the new S. American classification compared favourably with its forerunner. It can be correlated to the bacteriological and patho-anatomical findings. *P. Manson-Bahr*

See also p. 346, WESTERN AUSTRALIA, **Report of the Commissioner of Public Health for the Year 1947.**

CUNHA, R. A. O bacilo de Hansen. Morfologia e fisiologia. [**Morphology and Physiology of Hansen's Bacillus.**] *Bol. Serviço Nac. de Lepra.* Rio de Janeiro. 1944, Sept., v. 3, No. 3, 29–55.

A general review.

ROSSELL, C. S. C. Novos cultivos cromogênicos de bacilos ácido-alcool resistentes isolados de mosquitos (*Culicini*), capturados sobre leprosos. II nota. [**New Chromogenic Cultures of Acid-Fast Bacilli isolated from Culicine Mosquitoes fed on Leprosy Patients.**] *Mem. Inst. Oswaldo Cruz.* 1947, Dec., v. 45, No. 4, 793–812, 4 figs.

The English summary appended to the paper is as follows :—

"The author describes three new samples of cultures of acid-fast bacilli isolated from wild mosquitoes experimentally fed on active cases of leprosy, in the South of the State of Minas Gerais, about 1 mile distant from Santa Fé Leper Colony.

"All those cultures are chromogenic and germinate quite well on Loewenstein medium and in glycerinated broth, forming thin veil on the surface of this medium, without clouding it.

"Out of 100 slides smeared with intestinal contents from wild mosquitos fed on lepers, 22 were positive for acid-fast bacilli similar to those of Hansen, and out of 100 slides smeared with domicile mosquitos, captured in leper dormitories, 20 were also positive.

"Fifty smears from mosquitos captured on horses were negative for typical acid-fast bacilli."

CUNHA, R. A. Técnicas utilisáveis com o bacilo de Hansen e os soros leprosos. [**Bacteriological and Serological Methods used in the Diagnosis of Leprosy.**] *Bol. Serviço Nac. de Lepra.* Rio de Janeiro. 1944, Dec., v. 3, No. 4, 31–51. [160 refs.]

A general review.

DHARMENDRA & MUKHERJI, N. **Lepromin Reaction in Subsided Lepromatous Cases.** *Leprosy in India.* 1947, Jan., v. 19, No. 1, 5–10.

After summarizing previous work on this point, the authors record a careful study with illustrative tables of their experience in 17 out of 125 active cases

of leprosy in which a weakly positive lepromin reaction developed. In 8 of the 17 cases the subsidence of symptoms had persisted for 2 to 5 years ; in the other 9 a slight or marked relapse had occurred, with lesions becoming bacteriologically positive in half. Of the first series of 8 cases, the reaction changed to a doubtful or weak positive in 6. In the 9 cases in which relapse had occurred 7 negative and two weak positive reactions had been noted in the active stage ; after subsidence of the disease, in 5 the reaction remained negative and of the remaining 4 a decrease was noted in 2 and an increased reaction in the other 2. Relapses are therefore less frequent in subsided cases in which increased reactions were noted. *L. Rogers*

DHARMENDRA & JAIKARIA, S. S. **Failure to sensitize presumably Non-Leprous Individuals to Lepromin.** *Leprosy in India.* 1947, Jan., v. 19, No. 1, 16–17.

"We have, therefore, failed to confirm the findings of Fernandez that an injection of lepromin sensitizes lepromin-negative non-leprous persons so that they become lepromin-positive."

CUNHA, R. A. Serologia da lepra. [**Serology of Leprosy.**] *Bol. Serviço Nac. de Lepra.* Rio de Janeiro. 1944, Dec., v. 3, No. 4, 3–30.

A general review.

RABELO, F. E. A. Aspectos do diagnostico diferencial da lepra. [**Points in the Differential Diagnosis of Leprosy.**] *Bol. Serviço Nac. de Lepra.* Rio de Janeiro. 1945, Mar., v. 4, No. 1, 40–51.

This article is one of a series of notes for a course of lectures on leprosy for members of the National Health Service, apparently delivered, at all events prepared for, in 1942. This one deserves special mention because it brings together and points out in tabular form the differential diagnosis between leprosy and skin conditions which in one or more aspects resemble leprosy. Lack of space precludes their being recorded in detail here, but the general lines of treatment of the subject should be indicated. The diseases mentioned are : syphilitic roseola and leuco-melanoderma, polymorphic exudative erythema, erythema nodosum, centrifugal annular erythema, psoriasis, vitiligo and pinta. In each case, the site commonly involved is stated and the appearance, the course and the histology of the lesions. This information can be found in publications dealing with leprosy and the better works on cutaneous diseases, but it is very convenient to have them collected thus in a single contribution by a leprologist of repute. *H. Harold Scott*

CHAUSSINAND, R. La classification de la lèpre. [**The Classification of Leprosy.**] *Bull. Soc. Path. Exot.* 1948, v. 41, Nos. 3/4, 249–60.

RABELO, F. E. A. As formas clinicas da lepra sob o ponto de vista da epidemiologia e da profilaxia. [**Clinical Forms of Leprosy from the Epidemiological and Preventive Aspects.**] *Bol. Serviço Nac. de Lepra.* Rio de Janeiro. 1945, Mar., v. 4, No. 1, 28–39.

SILVEIRA, L. M. O mal perfurante plantar na lepra. [**Perforating Plantar Lesions in Leprosy.**] *Arquivos do Serviço Nac. de Lepra.* Rio de Janeiro. 1946, Dec., v. 4, No. 3, 182–203, 40 figs.

DE CASTRO, J. C. R. Las lesiones viscerales en la lepra tuberculoide como un nuevo elemento en el cuadro de la clasificación sud-americana. [**Visceral Lesions in Tuberculoid Leprosy.**] *Arquivos do Serviço Nac. de Lepra.* Rio de Janeiro. 1947, Apr., v. 5, No. 1, 132–42, 8 figs. [16 refs.]

Little, if anything, seems to be known concerning the occurrence of visceral lesions in patients with tuberculoid leprosy. The author has had under his care and observation a boy, 10 years of age, who had, at the age of 7½, noticed a spot in the middle of the front of his right thigh, with definite contour, red in colour. This increased in size from 1·5 to 8 cm. in diameter when a similar spot appeared on the lower third of his right arm, with alteration in sensibility, and later others on the left leg and foot. When the author saw him the maculae were about 12 cm. in diameter and there was diminished sensibility to heat and pain. Hansen's bacilli were seen in smears of the cutaneous lymph. Biopsy specimens were taken of the skin, the liver, a mesenteric gland, epiploon and the sternal marrow under a general anaesthetic. In the gland and epiploon *Myco. lepræ* were seen and in smears of the liver [but, later, under the description of the separate tissues is the statement that " bacteria were not met with on direct examination "]. In the tissues lymphocytic infiltration was observed, with eosinophil increase and histioid proliferation which the author interprets as indicating that tuberculoid leprosy is not confined to the skin and superficial glands but is a generalized condition affecting all the organs, setting up pathological processes different from those of the lepromatous form.

H. Harold Scott

RAJAH, Z. J., RAJ, M. P. & COCHRANE, R. G. **A Short Note on Experimental Investigations on the Optimum Dose of Hydnocarpus Preparations at the Lady Willingdon Leprosy Sanatorium, Chingleput, S. India.** *Leprosy in India.* 1948, July, v. 20, No. 3, 146–8.

Tests have been made to find the optimum dose of hydnocarpus preparations by the use of 10 cc., 10–15 cc. and 15–25 cc. respectively in different groups of cases, with the result that 15 per cent. became negative on the highest dose against only 9 per cent. on the lowest one, but as the lower-dose group included more advanced cases the test was repeated, with a better distribution of cases. This showed 18 per cent. became negative on the high, 33 per cent. on the medium and 24 per cent. on the lowest dose. Further tests were carried out with intradermal injection only, subcutaneous injection alone or both methods combined ; and the combination of methods gave the best results, which were confirmed by a repetition of the test.

L. Rogers

BECHELLI, L. M. & ROTBERG, A. Terapêutica chaulmoógrica da lepra. A eficiência do chaulmoogra, de acôrdo com o estudo de 2,201 casos de alta. [**Chaulmoogra in Leprosy. A Study of 2,201 Patients.**] *Arquivos de Serviço Nac. de Lepra.* Rio de Janeiro. 1946, Dec., v. 4, No. 3, 363–74, 1 graph.

This contribution analyses the 2,201 cases, some of which were referred to in the preceding abstract. Of 411 of the lepromatous type 224 had presented themselves with relapse, 165 remained out and apparently well, 12 had died, 8 had been transferred elsewhere and 2 had ceased to attend for treatment. Of 1,221 " non-characteristic ", 229 had relapsed, 898 were at liberty, 60 had died, 31 had gone elsewhere and 2 had ceased to attend ; of 569 of the tuberculoid form 57 had had relapses, 471 were up and about, 24 had died, 16 had been transferred and one discontinued treatment.

H. Harold Scott

ROTBERG, A. & BECHELLI, L. M. Terapêutica chaulmoógrica da lepra. Resultado do tratamento chaulmoógrico na lepra: observações pessoais e estudo de 2.201 casos de alta registrados em nosso serviço. [**Personal Observations on 2,201 Leprosy Patients treated with Chaulmogra Oil.**] *Arquivos do Serviço Nac. de Lepra.* Rio de Janeiro. 1946. Dec., v. 4, No. 3, 352–63, 7 figs.

For oral administration the pure oil was used and for intramuscular or intradermal injection the esters. The authors aimed at giving 100 cc. in 10–30 weeks, after which a rest of 15–20 days was interposed. When a total of 300 cc. is reached (in 40–100 weeks), 2–3 months are allowed to elapse before another course is started. In children the dose used is smaller, 1–2 cc. once or twice weekly, at times 3 cc., and the course is 100–200 cc. according to the tolerance.

A table is given showing the results in 679 cases of the lepromatous form. Of 101 receiving up to 100 cc. of the oil, 95 were worse, 5 were unchanged and one was better; of 92 receiving up to 200 cc. 76 were worse, 14 unchanged and 2 improved; 10 patients received more than 2,000 cc.; of these 8 were worse, 2 were better. Altogether of the 679, 581 (85·5 per cent.) were worse 75 (11·04) were unchanged, and only 23 (3·4) had improved.

Of the other forms, non-characteristic and tuberculoid, nothing definite is said, and the results would be difficult to gauge seeing that spontaneous remissions are fairly common in them. *H. Harold Scott*

FLOCH, H. Influence du traitement par l'huile de chaulmoogra sur l'évolution de la lèpre. [**Chaulmoogra Treatment and the Evolution of Leprosy.**] *Arquivos do Serviço Nac. de Lepra.* Rio de Janeiro. 1946. Dec., v. 4, No. 3, 257–70.

This paper deals with an analysis of 358 leprosy cases treated "more or less" for periods of 3 to over 12 years, with Chaulmoogra oil, with a view to determining the most efficient method of using the remedy. The first table shows ages and sexes. Bacteriological examinations, given in Table II, showed lepra bacilli on the skin in only 7 per cent. of 234 cases and none in the nose among 196 maculo-anaesthetic cases. In nerve cases, 1 of 34 was skin-positive only. On the other hand, 66 of 68 lepromatous cases were positive bacteriologically in skin leprosy. Chaulmoogra oil was given intramuscularly in varying total amounts and frequencies shown in another table, which brings out the important points that in maculo-anaesthetic cases given a total of over 300 injections, 60 per cent. were benefited against 45 per cent. in those who were not so treated. Among 34 nerve cases the progress was not influenced by the number of injections. In the lepromatous form, improvement was seen in 45 per cent. of those receiving an annual mean of 40 to 50 injections, but in very advanced cases the percentage fell to 25–30 per cent., as is shown in a table. The importance of long regular treatment is also shown in a table 40 per cent. of lepromatous cases benefited by treatment over the full period, as compared with 21 per cent. who improved with shorter periods of treatment. Thus the treatment is more effective when it is carried out regularly for long periods than it is with shorter periods and frequent interruptions. This is in accordance with other recent experience. In a final table, this is confirmed by the finding that 50 per cent. of those regularly treated for a sufficiently long period improved as compared with only 27 per cent. who had irregular treatment with long intervals, instead of regular weekly injections for a minimum of three years. *L. Rogers*

ROTBERG, A. & BECHELLI, L. M.; BECHELLI, L. M. & ROTBERG, A. Terapêutica chaulmoôgrica da lepra. Apanhado crítico sôbre a literatura do tratamento chaulmoôgrico da lepra. Ia Parte–5a Parte. [**A Critical Review of the Literature relating to Chaulmoogra Treatment of Leprosy.**] *Arquivos do Serviço Nac. de Lepra.* Rio de Janeiro. 1946, Dec., v. 4, No. 3, 313–19. [15 refs.]; 319–25. [22 refs.]; 325–32. [21 refs.]; 332–9. [24 refs.]; 340–47. [11 refs.]

ROTBERG, A. & BECHELLI, L. M. Terapêutica chaulmoôgrica da lepra. Fatôres a considerar na avaliação dos resultados da terapêutica antileprótica. 1a Parte. [**Factors in the Assessment of the Results of Anti-Leprosy Treatment, with special reference to Chaulmoogra. 1st Part.**] *Arquivos do Serviço Nac. de Lepra.* Rio de Janeiro. 1946, Dec., v. 4, No. 3, 291–300; 3 figs. & 2 graphs.

BECHELLI, L. M. & ROTBERG, A. Terapêutica chaulmoôgrica da lepra. Fatôres a considerar na avaliação dos resultados da terapêutica antileprótica. 2a Parte. [**Factors in the Assessment of the Results of Anti-Leprosy Treatment, with special reference to Chaulmoogra. 2nd Part.**] *Arquivos do Serviço Nac. de Lepra.* Rio de Janeiro. 1946, Dec., v. 4, No. 3, 300–313, 14 figs.

CHAUSSINAND, R., PARIS, C. & CROUGUE, O. Essais d'un traitement ambulatoire de la lèpre par la streptomycine, émulsionnée dans les esters éthyliques de chaulmoogra. [**Streptomycin with Chaulmoogra Esters in Leprosy.**] *Bull. Soc. Path. Exot.* 1948, v. 41, Nos. 9/10, 573–6.

This paper records a trial of streptomycin and chaulmoogra esters in two cases of leprosy. The first was an advanced lepromatous case with numerous lepra bacilli in the nose and in nodules, and of about 7 years' duration. Daily injections of 1 cm. chaulmoogra esters with streptomycin in doses rapidly increased from one-third of a million to two million U.S. were continued for 79 days, when they ceased to be absorbed. During that period a total of 42 million of U.S. units were given. A notable reduction of diffuse infiltration of the face and ears, but not of other cutaneous lesions, was noted, together with diminution of nasal lepra bacilli, but those in the nodules were unchanged. The improvement was not greater than with chaulmoogra esters alone in the period of treatment. A second case was therefore treated in the same manner: this patient had signs of cutaneous erythematous lesions of the lepromatous type with numerous lepra bacilli, but no infiltration. It was hoped that streptomycin might be more effective in such a comparatively early stage. The treatment was continued for 98 days, during which 135½ million units of streptomycin were given, together with chaulmoogra esters. Only a minimal modification of the cutaneous lesions was obtained and there was no diminution in the cutaneous lepra bacilli, although a slight bacterial infection of the nose cleared up. As far as these two cases go there was no definite evidence of any effect of the large and costly streptomycin treatment. [See also FAGET and ERICKSON, this *Bulletin*, 1948, v. 45, 442, 615.] *L. Rogers*

SOUZA LIMA, L. & CASTRO CERQUEIRA, G. de. Tratamento experimental da lepra pelas diaminno-di-fenil-sulfonas. [**Trial Treatment of Leprosy with Diamino-Diphenyl Sulphone.**] *Arquivos do Serviço Nac. de Lepra.* Rio de Janeiro. 1946, Dec., v. 4, No. 3, 9–76, 50 figs. on 25 pls.

The crucial test of all treatments of leprosy must be their results in lepromatous cases, because tuberculoid forms and many of the "non-characteristic" forms tend to retrogress spontaneously.

The author here puts on record the results of the use of diasone and promin. Diasone was given orally in capsules containing 0·33 gm. for 6 weeks, followed

by two weeks' rest. One capsule daily was given for 3–4 days, then two for the same period and after that three capsules, or 0·99 gm., for the daily dose. This drug was given to 38 patients, 12 in an advanced stage, 20 " moderate ", and 6 incipient cases.

Promin was administered intravenously to 42 patients, 17 advanced, 23 " moderate " and 2 incipient, starting with 1 cc., and gradually increasing to 5 gm. [so stated, but the strength of the solution is not mentioned]. The drug was given daily for 15 days, followed by 7 days' rest. The red cells were counted and the haemoglobin estimated every 10 days. The following criteria were observed for estimating results : 1. *Dermatological*—comparison of the cutaneous condition before and after and at intervals during the treatment. 2. *Histological*—comparison of the histo-pathological picture before and at intervals after. 3. *Bacterioscopic*—the numbers and characters of the bacteria in smears and sections of the skin lesions. 4. *Clinical*—the general condition, including the ophthalmological and the oto-rhino-laryngeal.

Each of these is recounted and discussed in detail and the results shown in an elaborate series of tables, but much more will be gathered from a study of the excellent photographs of patients before treatment and during and after the courses. The histological changes are also well shown by photomicrographs. The results may briefly be summarized thus : Of the 38 receiving diasone, all 12 in the advanced stage showed some improvement, 3 marked improvement, 8 were better and one slightly better ; of the 20 " moderate " cases 5 were much improved, 10 improved, 3 slightly better, 2 were unchanged ; and of the 6 incipient cases one was much improved and the other 5 improved.

With promin treatment : Of the 17 advanced cases, 6 were much improved, 9 improved, one remained unchanged and one was worse ; of 23 " moderate " cases 7 were much improved, 10 improved, 4 slightly better, 2 remained unchanged ; both the incipient cases were much improved. In other words, of the total 80, marked improvement was reached in 24, considerable improvement in 42, slight in 8 ; 5 remained unchanged and one only was worse. [The numbers in the text have been added wrongly.]

In their conclusions the authors state that the drugs are well tolerated by leprosy patients of any age and are free from danger, if ordinary precautions are taken ; that the drugs are active, clinically and bacteriologically, in the treatment of this disease, though the extent of this activity cannot at the moment be stated definitely ; that they act beneficially on the eye symptoms and on those due to affection of the nose and throat, and that they certainly exercise a bacteriostatic, and possibly a bactericidal action, and, finally, that they seem to be the most efficient of drugs at present known in the treatment of leprosy and that they should be more widely used. *H. Harold Scott*

FIGUEREDO, N.* & DESAI, S. D. **The Importance of Home Visits in the Control of Leprosy in Bombay City.** *Leprosy in India.* 1948, July, v. 20, No. 3, 149–52.

In 1941 the importance of home visits to follow up leprosy cases was emphasized and in 1942 the Clinic of the Ackworth Leper Home appointed two trained health visitors for this purpose, as 30 to 35 per cent. of the cases attending the clinic were ceasing to come. Moreover the examination of contacts was unsatisfactory, as was the separation of healthy children from infectious cases, many of whom could not be accommodated at the Ackworth Home. Visits of the health visitors to overcome these deficiencies during 1943 to 1947 amounted to nearly 14,000 and included the examination of over 7,000 contacts with the discovery of 445 suspected or clear cases of leprosy. Moreover 159 out of 412 patients were induced to resume attendance at the Clinic, which

had usually been stopped either on account of great improvement or a stationary condition. Much overcrowding was met with in the patients' homes and much useful advice was given. The visits were of value in many cases and they should be continued.

L. Rogers

JOSEPH, J. J. **Legislation on Leprosy in India.** *Leprosy in India.* 1947, Jan., v. 19, No. 1, 11–15.

The deformities produced by leprosy have led to severe laws in the past, the effects of which in reducing the incidence of the disease are very doubtful. Epidemic diseases may have reduced the numbers in the past. Sanitation and education may also have reduced the cases. The present time is favourable for more efficient legislation on an all-India basis in place of the present unsatisfactory laws. This should control infectious cases and protect susceptible children. Legislation should therefore provide All-India and provincial Control Boards with executive powers, the first of which should approve special Acts or Bills. Notification should only apply to infectious cases, which should be defined in the Bill. All medical men should notify cases confidentially and be liable to a penalty in default. Child contacts of infectious cases should be recorded and examined periodically and no infectious case permitted to live as co-tenant with other families. Marriages of infected should require sanction of the Control Board, but infection should not be a cause for divorce. Infectious prisoners should have separate accommodation. The use of the word " leper " should be prohibited. Unqualified persons should not give injections without permission of the medical department. Private-aided institutions will not be under a Leprosy Act ; they should be regulated if receiving Government grants. Infectious cases should be separated from untreatable advanced crippled nerve cases. All discharged infectious cases should be observed periodically for seven years. The views of leprosy workers should be discussed by a special committee and circulated to local governments for discussion before any legislative Act is passed.

L. Rogers

SIMONS, R. D. G. P. **Modern Conceptions concerning the Compulsory Isolation of Lepers. Contagious Malignant Morbus Hansen *versus* Non-contagious Benign Hansenide.** *Proc. Roy. Soc. Med.* 1948, Nov., v. 41, No. 11, 751–4 (Sect. Dermat. 27–30).

This is a good account of the modern method of isolating only the infective cases of leprosy in place of the old futile plan of segregating also the much larger number of uninfective types, with resulting hiding of all types until treatment could be of little avail. After dealing with modern methods of classification and the great infectivity of lepromatous cases, with enormous numbers of lepra bacilli, as compared with nerve and tuberculoid cases with very few, the author quotes the data of ROGERS to show the former to be twenty times as infective as the latter. He classes cases as (1) the contagious malignant form and (2) the non-contagious benign form, and states that of the latter " their segregation is unscientific, unreasonable and inhuman " as " the whole weight of modern, competent opinion is that such cases (*i.e.* 80 per cent. of all (Rogers)) are no danger to the public and that their segregation only encourages false and misleading fear ". He also points out that the recognition of these facts in the new terminology should give a new lease of life to the N or T patients and " *the ghastly alternatives of either no medical treatment or barbed wire for life would no longer confront them* ". These types should therefore be released and sent to a home or sanatorium for treatment with great saving of expense.

The contagiousness of leprosy is next discussed and a number of cases of accidental inoculation of the infection are quoted. Infection through contact is pretty certainly due to close and long association, so it is largely a " familial disease " with relatively low infectivity. The bed bug is a more likely carrier than the cockroach. The Nauru epidemic is quoted as an example of control by isolation only of the bacteriologically positive infectious cases, and South African experience as a demonstration of the much greater effectiveness of the modern plan of only isolating with effective treatment infectious cases coming forward in the early stages of the disease. The author concludes that : " To-day, however, there remains no doubt that one can save energy and money by isolating only the malignant lepromatous and NOT the Hansenite [uninfective] patients ".

L. Rogers

McCoy, G. W. **Leprosy : Factors in Public Health Management.** *Pub. Health Rep.* Wash. 1948, Nov. 19, v. 63, No. 47, 1522–6.

This paper deals with the prophylactic measures, from the American point of view. The author first states that : " We hope that by now the routine control procedure—isolation of all cases of leprosy regardless of the possibility that some patients may not be a menace to their associates—has been discarded . . . as there is no substantial evidence that it aided in controlling infection." The value of promising therapeutic agencies (sulphones) first tried by G. H. Faget and his associates, will, it is hoped, lead to earlier and more effective treatment. Only the lepromatous and mixed lepromatous and neural types are likely to be sources of infection and to require isolation. Neural and anaesthetic cases are relatively free from danger of transmitting infection and should receive the benefit of the doubt and not be compulsorily isolated. The tuberculoid sub-type is also unlikely to be transmitted.

In diagnosis it is pointed out that in nasal smears a few non-leprous acid-fast bacilli may sometimes be found, but bundles of such organisms are of diagnostic value. Histological changes may be misleading unless lepra-bacilli are present. Cases with nerve symptoms who have never lived in a leprous area, are very unlikely to be leprosy. The disease in the U.S.A. is only a problem in the southern Gulf of Mexico States. From the public health point of view, the author advises that no special consideration is required for non-communicable cases where transmission is unlikely ; home isolation or general hospital care are recommended for any cases where transmission is unlikely, and special hospitals for communicable cases where spread is likely to occur.

L. Rogers

Ashbel, R. & Poljakoff, A. **In Vitro Cultivation of the Rat Leprosy Organism.** *J. Infect. Dis.* 1948, Nov.–Dec., v. 83, No. 3, 279–82, 1 fig.

Chaussinand, R., Paris, C. & Crougue, O. Essais de traitement par la streptomycine de l'infection murine due au bacille de Stefansky. [**Trials of Streptomycin in Rat Leprosy.**] *Ann. Inst. Pasteur.* 1948, July, v. 75, No. 1, 92–4.

The direct action of streptomycin on Stefansky's bacillus of rat leprosy cannot be tested because that organism has not been cultivated, but the preparation did not have any effect *in vitro* in altering the appearances of the bacilli or their staining properties. Further, rats inoculated with the rat leprosy bacilli which had been exposed to the action of streptomycin were readily infected in a similar manner, as with the untreated organism. The action of the preparation was then tried *in vivo* by treating 30 infected rats with streptomycin and keeping 15 more as controls. The treatment was commenced

two and a half months after inoculation, when infiltration could just be detected at the site of infection. Daily doses of 4,000, 6,000 and 8,000 U.S. units respectively were injected subcutaneously every other day for two months and the rats were killed from two to seven months after commencement of the treatment, but the lesions observed were similar in the treated and untreated rats. The drug was then given to another series of animals up to doses of 16,000 units as before, but commencing two days after inoculation with rat leprosy bacilli ; again no differences were found in the degree of infection after two to seven months. A further test in the more resistant mice also gave negative results ; a total of 190 rats and 40 mice being tested. Streptomycin may therefore be classed as ineffective against Stefansky's bacillus of rat leprosy.

L. Rogers

HELMINTHIASIS

Brown, M., Sinclair, R. G., Cronk, L. B. & Clark, G. C., with E. Kuitunen-Ekbaum. **Intestinal Parasites of Eskimos on Southampton Island, Northwest Territories. A Preliminary Survey.** *Canadian J. Pub. Health.* 1948, Nov., v. 39, No. 11, 451–4.

" A study of intestinal parasites among 95 Eskimos on Southampton Island, N.W.T., showed that 33 individuals, or 34·7 per cent., were infected with the following parasites : *Enterobius vermicularis* (22 cases), *Diphyllobothrium* sp. and *E. vermicularis* (3 cases), *Diphyllobothrium* sp. (6 cases), *Endamoeba coli* (1 case), *Giardia lamblia* (1 case). The specimens examined were 83 NIH swabs and 31 faecal samples.

" A varying degree of blood eosinophilia, up to 56 per cent., was found in 79 cases examined. There appeared to be no relation between the percentage of eosinophils and the parasitological findings recorded."

Rodriguez M., J. D. Parasitismo intestinal en los escolares de Guayaquil. [**Intestinal Parasitism in Schoolchildren in Guayaquil.**] *Rev. Ecuatoriana de Hig. y Med. Trop.* Guayaquil. 1944, July, v. 1, No. 3, 251–4.

Alvarez Crespo, J. Parasitismo intestinal en enfermos hospitalarios de Guayaquil. [**Intestinal Parasites in Hospital Patients in Guayaquil.**] *Rev. Ecuatoriana de Hig. y Med. Trop.* Guayaquil. 1944, Apr., v. 1, No. 2, 203–10. [23 refs.]

Hsu, K. C. **A Survey of the Helminths of Dogs in Chengtu, Szechuan.** *Chinese Med. J.* Shanghai. 1948, July, v. 66, No. 7, 366–70. [19 refs.]

" (1) A survey of the helminths of 169 dogs in Chengtu was conducted and every dog was found to be infested. The number of species of parasites harbored by each dog varied from 1 to 7.

" (2) The percentage of dogs harboring round worms was found to be 90·5 per cent. They were *Ancylostoma caninum*, *Ancylostoma braziliense*, *Uncinaria stenocephala*, *Toxocara canis*, *Spirocerca sanquinolenta*, *Dirofilaria immitis*, and *Thalazia callipaeda*.

" (3) The percentage of dogs harboring cestodes was 69·7 per cent. They were *Taenia hydatigena*, *Diphyllobothrium mansoni*, and *Dipylidium caninum*.

" (4) The percentage of dogs harboring trematodes was 8·2 per cent. They were *Clonorchis sinensis*, *Paragonimus* spp., *Metagonimus yokogawai*, and *Microtrema truncatum*.

" (5) *Microtrema truncatum* is reported probably for the first time as occurring in dogs in China."

PANAYOTATOU, Angelique. Nouvelles recherches sur la " Bilharziose Vesicale " causée par (*Schistosoma haematobium*) guéris par l'antimonio-thiomalate de lithium. [**Studies of *Schistosoma haematobium* Infections cured by Anthiomaline.**] *J. Roy. Egyptian Med. Ass.* 1943, Feb., v. 26, No. 2, 66–71. [Recd. 13 Dec., 1948.]

MALDONADO, J. F. & ACOSTA-MATIENZO, Josefina. **Biological Studies on the Miracidium of *Schistosoma mansoni*.** *Amer. J. Trop. Med.* 1948, Sept., v. 28, No. 5, 645–57.

The authors carried out experimental studies on the hatchability, longevity and infectivity of the miracidia of *S. mansoni*, under controlled laboratory conditions. The material used and the experimental procedure are described in detail.

Hatching.—Few miracidia emerged in the first hour, but on exposing the eggs to artificial light, hatching proceeded rapidly. Out of 1,971 eggs, 1,660, or 83·6 per cent. hatched out. Of these, 65 per cent. did so during the first eight hours and 24 per cent. in the following 16 hours. Thus in the first 24 hours, 89 per cent. of the hatching was completed. During the second 24 hours, about 9·5 per cent. hatched and the remaining 1·5 per cent. hatched early on the third day.

Longevity.—Percentage mortality rates among similar batches of miracidia kept from one to nine hours respectively were as follows :—8·6, 13·6, 21·5, 34·9, 32·3, 60·9, 62·7, 74·7 and 100. The average span of life was between 5 and 6 hours. The longevity of miracidia which hatched in the first 24 hours was observed to be greater than that of miracidia which hatched after a long time.

Infectivity.—Snails (*Australorbis glabratus*) were exposed to miracidia for varying periods after hatching and their infectivity was estimated on the basis of observed penetration or failure to find the miracidia in the vessels after exposure. Of 103 miracidia exposed to the snail immediately after hatching, 71·8 per cent. penetrated. This proportion gradually decreased to zero within 8 to 9 hours of free life.

The sites of penetration were observed in a batch of 110 miracidia. Of these, 66·3 per cent. chose the head-foot organ ; 27·3 per cent. the tentacles and 6·4 per cent. the mouth collar. *J. J. C. Buckley*

DA SILVA, J. R. Contribuição ao estudo das formas evolutivas da esquistosomiase mansoni. [**Contribution to the Study of the Clinical Evolution of Infestation by *Schistosoma mansoni*.**] *Rev. Brasileira Med.* Rio de Janeiro. 1948, Nov., v. 5, No. 11, 794–802, 5 figs. [23 refs.] English summary.

In the clinical study of schistosomiasis it is clear that the parasitic activity is all-important. To determine this, the viability or otherwise of ova passed in the faeces is not a reliable guide, but a study of the ova obtained by rectal biopsy is. Eggs thus obtained may be living or dead ; if living they may be mature or immature, or may show altered development, and in gauging the results of treatment examination of the ova may show whether they have died shortly before, some time before and become calcified, or have left empty shells. The action of specific drugs is not, it is believed, upon the eggs themselves directly, but upon the female worms, preventing oviposition. Hence, rectal biopsy and examination of ova so obtained are of value in assessing the results

of treatment; in some of the cases referred to, ova obtained by rectal biopsy, several months after treatment, were found to be still viable; clearly the treatment had been ineffectual. *H. Harold Scott*

GELFAND, M. & ROSS, W. F. **The Diagnosis of Schistosomiasis by Rectal and Vesical Snips based on 150 Autopsies.** *J. Trop. Med. & Hyg.* 1949, Jan., v. 52, No. 1, 12–15.

In S. Rhodesia MEESER, ROSS & BLAIR [this *Bulletin*, 1948, v. 45, 794] have shown the superiority of rectal biopsy over the use of Weller's scraper in the diagnosis of rectal schistosomiasis. GELFAND [this *Bulletin*, 1949, v. 46, 56] has demonstrated, post mortem, the efficacy of the examination of snips from the bladder in the diagnosis of *S. haematobium* infestations. In the present paper the diagnostic value of examination (post mortem) of snips from the bladder and from the rectum is further demonstrated; the conclusion is reached that biopsy from the bladder or rectum is warranted in clinical practice to establish a diagnosis of schistosomiasis. The authors supply the following summary :—

" (1) A comparative study is made of 150 cases of schistosomiasis in which bladders and rectums were removed at post-mortem, snips being taken from these organs prior to their digestion in caustic potash.

" (2) The bladder snips were positive for *S. haematobium* in 80 per cent. of known cases of *S. haematobium* infection and the rectal snips were positive for *S. mansoni* in 52 per cent. of known cases of *S. mansoni* infection.

" (3) *S. haematobium* infection was diagnosed by rectal snip in 60 per cent. of cases.

" (4) These results confirm the value of vesical snips in the recognition of *S. haematobium* in bladder infestations and also the relative frequency in which *S. haematobium* infections may be recognised by rectal snips.

" (5) The results also confirm our previous experience that pure *S. mansoni* infections are extremely uncommon in South Central Africa."

A. R. D. Adams

CHANG, T.-H., SMITH, G. W., RIESENMAN, F. R. & ALSTON, E. F. **Cerebral Granuloma due to Schistosomiasis.** *J. Amer. Med. Ass.* 1948, Jan. 24, v. 136, No. 4, 230–38, 7 figs. [Refs. in footnotes.]

The authors were able to collect references to 23 cases of cerebral schistosomiasis prior to 1946; from 1946 onwards, 15 additional cases, including 4 by CARROLL [this *Bulletin*, 1946, v. 43, 1047] and 6 by TILLMAN [*ibid.*, 1947, v. 44, 600], have been reported. Of these 38 cases, in 28 the diagnosis was presumptive, on clinical evidence combined with pathological bowel findings, in 5 it depended on biopsy findings and in 5 on autopsy. In 3 cases, *Schistosoma haematobium* was the parasite concerned and in 35 *S. japonicum*. In no case were *S. mansoni* eggs found in the brain.

The authors report two further cases :—

Case 1.—An ex-service man aged 26, who had been on Leyte, was seen on August 13th, 1945, with weakness of right arm and leg, dysphagia, blurring of vision, weakness of the right facial nerve and a low-grade fever, all of a few days' duration. By September 7th, the weakness of the limbs had improved slightly but he was suffering from severe headaches. Hyperaesthesia and hyperreflexia were noted. He had a 12 per cent. eosinophilia. By April 1946, there was further improvement in the paresis and hyperaesthesia, but the patient had developed complete motor aphasia. A craniotomy was

performed on April 12th. The dura was adherent to the posterior portion of the third middle frontal convolution and on the surface of the inferior frontal convolution a number of nodules, from pin-point to 2 mm. in diameter, were observed. Biopsy showed *S. japonicum* ova. There was immediately some improvement and this continued after three courses of stibophen (of 14 injections each with 5 ml. as the maximum dose); however, he had several Jacksonian fits. By May 20th 1947, the only residue was minimal aphasia. No schistosome ova were found elsewhere in this patient.

Case 2.—An ex-service man, aged 22, with service in Leyte, gave a history of attacks of unconsciousness with left-sided twitchings, preceded by numbness of the left knee and headaches. He was first seen on December 22nd, 1946. The subsequent seizures all involved the right side and he did not lose consciousness. On examination between attacks he had slight weakness of the right grip, some incoordination of movement on the right side, a positive Romberg sign, and a tendency to adduct the right leg when walking.

At craniotomy on February 25th, 1947, a fronto-parietal flap was made on the left side. The posterior portion of the dura was adherent and yellowish-white masses of 2·5 mm. were seen on the underlying convolution. These were resected and *S. japonicum* ova were found as in the previous case. The patient was aphasic after the operation but recovered slowly. He was given a course of stibophen starting on March 19th and by May 20th he was free of all neurological signs.

Dr. G. M. SAUNDERS, in a personal communication to the authors, reported two similar cases in which neurological localizing signs developed and craniotomy was performed, in one case with complete relief of symptoms, in the other with only partial. Stibophen was also given when schistosome ova were demonstrated in the biopsy.

In a discussion, in which the authors describe the life cycle of the worm, they note that cerebral complications are more common in the third stage of the disease than earlier. Quoting CARROLL (*loc. cit.*) they state that the symptoms are usually somewhat different at the two stages. Within the first 6 months of infection, there is usually drowsiness followed by coma and incontinence. There may be signs of pyramidal tract involvement with weakness, spasticity, exaggerated reflexes, an extensor Babinski's sign, a high eosinophilia, and fever. The symptoms tend to subside with the cessation of fever. On the other hand, in the third stage, Jacksonian convulsions and hemiplegia are more common.

The authors point out that patients with cerebral schistosomiasis very frequently give no history suggesting the early manifestations of the disease and the diagnosis is often dependent on the biopsy findings. They consider that craniotomy is indicated as well as medicinal treatment, stibophen for preference.

L. E. Napier

GHAREEB, A. A. **Cancer of the Body and Tail of the Pancreas with Bilharziasis.** *J. Roy. Egyptian Med. Ass.* 1941, July, v. 24, No. 7, 311–20, 2 figs. [12 refs.] [Recd. 13 Dec., 1948.]

Report of a case.

WOOD, E. A. **Cough following Intravenous Tartar Emetic.** *J. Roy. Egyptian Med. Ass.* 1943, Feb., v. 26, No. 2, 54–64. [Recd. 13 Dec., 1948.]

ASHKAR. **The Effect of Tartar Emetic Treatment on the Liver and its relation to Jaundice.** *J. Roy. Egyptian Med. Ass.* 1944, Aug., v. 27, No. 8, 391–9, 1 graph. [10 refs.] [Recd. 13 Dec., 1948.]

HALAWANI, A. **On Fantorin in the Treatment of** *Schistosomiasis*. *J. Roy. Egyptian Med. Ass.* 1941, July, v. 24, No. 7, 342–7. [Recd. 13 Dec., 1948.]

"1. Fantorin is apparently similar in its chemical composition to Fouadin.

"2. 39 cases were treated with Fantorin as described in the text. Thirty-nine cases were apparently cured after completing their courses. One case proved refractory to treatment with Tartar Emetic and Fantorin.

"3. According to our observations, the effect of Fantorin on the course of the disease is favourable and no serious symptoms have been produced by it."

WATSON, J. M., ABDEL AZIM, M. & HALAWANI, A. **Investigations on Miracil D Nilodin and its Effect on Human Bilharziasis.** 70 pp., 2 graphs. [25 refs.] 1948. Cairo: Ministry of Public Health.

For abstract of this work, see this *Bulletin*, 1948, v. 45, 1018.

KHALIL Bey, M. & HILMY, I. S. **Report on the Progress of the Eradication of Bilharzia from Teftiche Wadi Kom-Ombo, Egypt.** *J. Roy. Egyptian Med. Ass.* 1942, Sept.–Oct., v. 25, Nos. 9/10, 264–80, 5 graphs. [Recd. 13 Dec., 1948.]

GÁLVEZ FERMÍN, N. Fascioliasis del Colédoco. [Reporte de un caso operado.] [**Fascioliasis of the Bile-Duct. Report on a Case treated by Operation.**] *Rev. Kuba Med. Trop. y Parasit.* 1948, Sept.–Oct., v. 4, Nos. 9/10, 191–2, 1 fig.

CALVO FONSECA, R. Hallazgo de *Blastocystis hominis* y quistes de *Endamoeba coli*, asociados a *Fasciola hepatica*, en bilis obtenida por intubación duodenal. [Nota clínica.] [**Detection of** *Blastocystis hominis* **and Cysts of** *Entamoeba coli*, **associated with** *Fasciola hepatica* **in Bile obtained by Duodenal Intubation.**] *Rev. Kuba Med. Trop. y Parasit.* 1948, Sept.–Oct., v. 4, Nos. 9/10, 193–4.

JOYEUX, C. Les phénomènes d'immunologie dans les helminthiases considérés chez les cestodes de l'homme. [**Immunological Problems in Helminthic Infections with special reference to Cestode Infections in Man.**] *Méd. Trop.* Marseilles. 1948, July-Aug.-Sept.-Oct., v. 8, No. 4, 463–70. [27 refs.]

Joyeux discusses various aspects of natural immunity and acquired immunity in relation to helminthic infections in general and then considers these phenomena in certain cestodes of medical interest. They are discussed under two headings, large and small cestodes, in the light of a previous suggestion that the size of helminths may be a factor in determining the "saturation point" in helminthic infections; in other words, the protection given to a host against acquiring an unlimited number of helminths owing to continuous exposure to infection.

Large cestodes.—Premunition is especially evident in the case of *Taenia saginata* and *T. solium*, in which infections with a single worm are the general rule, though on rare occasions multiple parasitism has been observed. In one case of the latter kind, the worms were reduced in size and the number of segments was less than normal. *Diphyllobothrium latum* differs from the Taeniid cestodes in that it is not restricted to the human host and commonly occurs as a multiple infection. Moreover, there is some evidence that this worm induces an immunity of a kind more resembling true acquired immunity than premunition. In infestation with the related non-human pseudophyllids, *D. erinacei* and *Ligula intestinalis*, premunition is absent in the former but present in the latter. It is concluded that zoological affinities are unconnected with protection phenomena in the cases cited.

Small cestodes.—It is known that mice are protected by the first infection with *Hymenolepis nana fraterna*, from subsequent infections with this species, but the human form of this parasite, *H. nana*, apparently induces no such response in the human host, judging from the enormous numbers of worms which have been found and which must have been acquired in successive infections. It is suggested that the difference in the volume of the human intestine from that of the rodent may be a contributory factor, and this recalls the idea of a " saturation point " previously postulated. *H. diminuta* occurs in the intestine of rats in fair numbers but premunition has been demonstrated in this infection, so that it is necessary to invoke the probability of a simultaneous ingestion of a number of larval stages ; this is facilitated by the fact that the intermediate host often harbours several larvae.

In conclusion, the author sums up that in addition to natural immunity (" *spécificité parasitaire* "), premunition and acquired immunity are represented in certain helminthic infections, but the manifestations of the latter are sometimes inexplicable and do not conform to bacteriological conceptions of immunity. *J. J. C. Buckley*

OBRADOR, S. **Clinical Aspects of Cerebral Cysticercosis.** *Arch. Neurology & Psychiatry.* 1948, Apr., v. 59, No. 4, 457–68.

Cerebral cysticercosis is common in Latin America : in Mexico ROBBS reported 25 cases in a series of 100 cases of cerebral tumour and in Chile, ARANA and ASENJO (this *Bulletin*, 1945, v. 42, 908) reported 25 in a series of 202 cases of intracranial tumour. The author collected 17 cases during 5 years of neurosurgery in Mexico ; of these 10 were confirmed at autopsy.

Cerebral cysticercosis can be classified as follows :—

1. Cortical.
2. Ventricular : (*a*) Isolated, (*b*) Multiple.
3. Basilar : Predominantly in (*a*) region of the cisterna magna, (*b*) cerebello-pontine angle, (*c*) anterior and middle fossae.
4. Mixed general and diffuse.

The main symptons of cerebral cysticercosis fell into four groups, epileptiform attacks, signs of increased intracranial pressure, mental disturbances, and loss of vision, according to the localization of the cysticerci. There is often pronounced cortical atrophy ; this and other observations make the author consider the possibility of some " toxic " action of the cysticerci.

The course of the disease is sometimes rapid, especially in children, with " fever, headaches, convulsions, vomiting and other acute and generalized neurologic signs." Or it may be irregular with intervals as long as 20 years between the appearance of different signs. More characteristically there are irregular and diverse neurological symptoms of a slowly progressive nature.

X-ray study of the skull gives both non-specific evidence, mainly evidence of increased pressure, and specific evidence, multiple diffuse calcifications : these were observed in one-third of the author's cases. Rarely, the cysts produce erosions of the bone. Encephalograms and ventriculograms may contribute to the diagnosis : *e.g.* hydrocephalus associated with cerebral atrophy is fairly typical of cysticercosis. Contributory evidence may be obtained by the demonstration of calcified cysticerci in other parts of the body.

Contrary to the experience of the British school, the author has found valuable evidence from the cerebrospinal fluid. [In a footnote it is stated that the section on the cerebrospinal fluid was written by Dr. D. NIETO from all his own 27 cases.]

The non-specific changes in 27 cases consisted of an increase in the cellular count 15 to 100 per cmm. with eosinophils varying from 0·5 to 33·0 per cent.,

an increase in total protein up to, but rarely above, 100 mgm. per 100 ml., an increase in globulin and a decrease in the glucose content to below 50 mgm. per 100 ml. The Wassermann reaction was negative.

The specific indication is given by the complement fixation test with an alcoholic extract of cystercerci from the pig. The reaction is done on the same lines as the Wassermann reaction, and in the author's 27 cases 2 were positive with 1 ml., 10 with 0·5 ml. and 15 with 0·2 ml. [The contrast between British experience, of cysticerci of Asiatic origin, and the Latin American experience suggests that either the latter are not reporting the milder cases of cysticercal epilepsy so commonly encountered here, or we are failing to diagnose more severe cases with signs of cerebral tumour or with predominantly psychotic symptoms. The milder epilepsy cases would not of course come into the hands of neurosurgeons. On the other hand, it is possible that we are not paying enough attention to the cerebrospinal fluid in suspected cases.]

L. E. Napier

Rodriguez López-Neyra, C. Bibliografia Equinococósica Ibérica. **A Spanish and Portuguese Bibliography of Hydatid Infection.** *Archivos Internac. de la Hidatidosis.* Montevideo. 1947, Dec., v. 7, Nos. 1/2, 131–74.

Arana Iñiguez, R., Garcia Capurro, R. & Caubarrere, N. L. Hidatidosis vertebral. A propósito de un caso diagnosticado precozmente. [**Vertebral Hydatids. Early Diagnosis of a Case.**] *Archivos Internac. de la Hidatodosis.* Montevideo. 1947, Dec., v. 7, Nos. 1/2, 243–55, 7 figs. [12 refs.]

Schroeder, A. Diagnóstico de quiste hidático cerebral. [**Diagnosis of Cerebral Hydatid Cysts.**] *Archivos Internac. de la Hidatidosis.* Montevideo. 1947, Dec., v. 7, Nos. 1/2, 195–218, 9 figs. & 2 pls. [31 refs.]

A full discussion.

Schlanger, P. M. & Schlanger, Henriette. **Hydatid Disease and its Roentgen Picture.** *Amer. J. Roentgenol. & Radium Therapy.* 1948, Sept., v. 60, No. 3, 331–47, 46 figs. [41 refs.]

To obtain the full value from this paper, it will be necessary to refer to it in the original, since there are 48 excellent skiagrams around which the paper is written. The authors have studied 120 cases of hydatid disease and they have added skiagrams from Professor B. N. Calcagno's series of 350 cases.

The order of frequency of the localization of primary hydatid cysts is the liver (55 to 65 per cent.), the lung (17 to 24 per cent.), the bones, the kidney, and the spleen, but practically any organ may be involved.

The liver cyst is the only one that is frequently calcified. Calcification does not indicate the death of the *Echinococcus* nor does it preclude infection at a later date, but the authors have never seen a calcified cyst enlarging. The X-ray appearance may be that of a completely calcified round or oval mass or of a rounded reticulated shadow, with or without a sharply defined segment of a circle at one part of the periphery. The liver is always enlarged, the right side of the diaphragm is raised, often divided into two arches, and its movement is limited. Cysts bulging from the lower surface of the liver often show a crescentic-like displacement of the barium-filled hollow viscera. Infected cysts usually show a fluid level. Ruptured cysts give a variety of appearances according to whether they have ruptured into the bronchial tree ("reactive" pneumonia), into the duodenum *via* the biliary ducts, directly into the digestive tract (reflux of barium into the cyst cavity), into the peritoneum, or through the skin.

Cysts occurred in the lungs in 22 per cent. of the authors' cases. They were usually of considerable size and caused a bulging of the thoracic cage, but no erosion of the ribs is seen in extra-pulmonary cysts. They often lose their round shape and become polycystic. They do not usually calcify. Diagnosis is best made by a bronchogram; the bronchi and bronchioles appear as the fingers of a hand grasping the tumour, and the smallest bronchioles may be obstructed and end in a point. Rupture can sometimes be foretold by the appearance of pericystic emphysema. Clinically this is associated with slight haemoptyses.

There were 4 cases of bone hydatid in the authors' series and 30 in Professor Calcagno's. The bone is "blown up and riddled with cavities"; there is no reparative reaction in the bone. Cysts of the spleen and kidney are difficult to differentiate clinically, but can usually be diagnosed by X-rays. Sometimes they are calcified. Cysts of the abdominal cavity are usually secondary to a ruptured liver cyst: the rupture may easily escape diagnosis at the time. After an interval, multiple cysts develop. Clinically the abdomen feels like a sack of potatoes and X-rays show innumerable "rounded shadows of the same density as the kidney." *L. E. Napier*

Prat, D. Complicaciones y secuelas del quiste hidático. Es la hidátidosis una afección benigna como se le ha considerado hasta hace poco? [**Complications and Sequelae of Hydatidosis. Is this so Benign an Affection as it has been regarded until recently?**] *Archivos Internac. de la Hidatidosis.* Montevideo. 1947, Dec., v. 7, Nos. 1/2, 15–26, 5 figs.

Though this article contains little, if anything, really new, it will serve a useful purpose if only it succeeds in impressing upon Uruguayan people in general that hydatids are not the benign, almost negligible, infestation to which they have paid but scant attention. The author quotes cases and gives illustrations of specimens from autopsies in which a neglected hydatid of the liver, for example, has led to an obstinate, even permanent, fistula or to rupture into the lung which could only be cured by the dangerous operation of lobectomy. *H. Harold Scott*

Halawani, A., Nor-el-Din, G. & Shaker, M. **An Investigation of a Localised Epidemic of Acute Hookworm Disease.** *J. Roy. Egyptian Med. Ass.* 1944, Aug., v. 27, No. 8, 294–302. [11 refs.] [Recd. 13 Dec., 1948.]

Kyle, L. H., McKay, D. G. & Sparling, H. J., Jr. **Strongyloidiasis.** *Ann. Intern. Med.* 1948, Dec., v. 29, No. 6, 1014–42, 9 figs. [52 refs.]

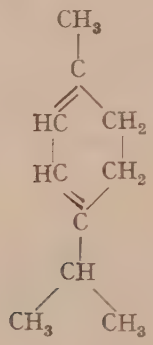
"A fatal case of *Strongyloides stercoralis* is presented. The filariform larvae were found in the usual locations and in addition were found in the myocardium, lungs, trachea, liver and gall-bladder.

"The clinical manifestations of this infection are variable but in general they include abdominal pain, alternate diarrhoea and constipation, cough, dyspnea and hemoptysis.

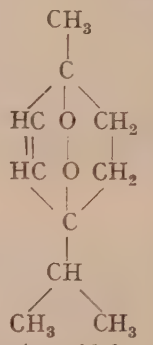
"Treatment with various drugs produces variable results. The best treatment to date is probably found in the use of gentian violet, given orally at first. If the infection is not cured by oral administration, intraduodenal and possibly intravenous administration should be tried."

SCHENCK, G. O. & SCHULZE-BUSCHOFF, H. Synthetisches Askaridol, eine neue Möglichkeit der Spulwurmbehandlung. [**Synthetic Ascaridol in the Treatment of Ascaris Infestation.**] *Deut. med. Woch.* 1948, Aug. 13, v. 73, Nos. 29/32, 341–4, 1 fig. [10 refs.]

Though ascaridol was isolated many years ago as an active principle of oil of chenopodium, constituting as much as 60 and even 80 per cent. of a good sample, attempts to synthesize it have until recently met with no success. Now this has been done by the catalytic action of chlorophyll on α-terpenes in the presence of light, resulting in the incorporation of oxygen as shown in the accompanying formula :



α-terpene



Ascaridol

The product is found, both chemically and physically, to be identical with the natural one. The relative toxicities were tested on mice and were found to be almost the same, the minimal lethal dose of the natural product being 0·157 gm./1000 gm. mouse and the absolute lethal dose 0·21 gm., whereas the relative amounts of Schenck's synthetic product were 0·16 and 0·22 gm. Tested on *Toxocara cati* the two were equally vermicidal.

Twenty-five human cases, all in adults whose ages ranged between 13 and 69 years, are recorded (in tabular form) of its use in the following way : A castor oil or saline purgative in the evening ; the next morning two capsules each containing 0·2 gm. of the ascaridol were given at 8 a.m. and a third at 8.30 a.m., 0·6 gm. in all. Breakfast at 10 a.m. consisting largely of vegetables and at 11 a.m. a castor oil purge. On the three succeeding days a dose of Carlsbad salts is given. One man, of 52 years, expelled 496 ascarides and all appeared to be dead. The dosage for children is set down as : 2–3-year-olds 0·1 gm., 3–4 years 0·2 gm., 5–6 years 0·3 gm. and 6–12 years 0·45 gm. These are the total dosages. In many cases a follow-up reveals no more passing of ova, but it is advised that, if the treatment needs to be repeated, an interval of 14 days should be allowed to elapse. No untoward side-effects have been reported or observed. *H. Harold Scott*

SCHUBERT, R. Erfahrungen mit dem synthetischen Askaridol "Schenck." [**Experiences with Synthetic Ascaridol "Schenck."**] *Deut. med. Woch.* 1948, Aug. 13, v. 73, Nos. 29/32, 344–5.

This author has tried the synthetic ascaridol prepared by Schenck, as above, on 35 patients with ascariasis. He reports very favourably on his results. In six only were ova seen after the treatment and these cleared finally, though oil of chenopodium had been given without effect previously. One patient had to have a second course of treatment. *H. Harold Scott*

OLIVER-GONZALEZ, J., SANTIAGO-STEVENSON, D. & HEWITT, R. I. **Treatment of Six Cases of Ascariasis in Man with 1-Diethyl-Carbamyl-4-Methylpiperazine Hydrochloride.** *Southern Med. J.* 1949, Jan., v. 42, No. 1, 65–6.

" Six patients infected with *Ascaris lumbricoides* were treated with 1-diethyl-carbamyl-4-methyl-piperazine hydrochloride (' hetrazan '), at 2 mg. per kg. given three times during a twenty-four-hour period at eight-hour intervals. All worms were apparently removed from three patients. The majority of worms were removed from the remaining three patients, as demonstrated by egg count reductions after treatment of 83·4, 91·3 and 99·5 per cent., respectively. Living worms were passed in all cases. The compound produced no toxic effects in the doses used."

RABEE, A. A. **Abdominal Section for Intestinal Obstruction due to 2005 Ascaris Worms.** *J. Roy. Egyptian Med. Ass.* 1943, Sept., v. 26, No. 9, 325–6. [Recd. 13 Dec., 1948.]

Report of a case.

BRUMPT, E. Filarioses et éléphantiasis. [**Filariasis and Elephantiasis.**] *Liber Jubilaris J. Rodhain* (*Soc. Belge Méd. Trop., Brussels*). 1947, Dec., 103–20.

To explain the absence or rarity of microfilariae in patients suffering from elephantiasis, it would be necessary (i) to accept Manson's view that the recurrent attacks of fever had killed the adult filariae : this is not very probable because, among healthy carriers, the worms persist in spite of more or less frequent attacks of fever, due for example to malaria : or (ii) to put forward the hypothesis that there is an antagonism in individuals between the conditions favourable for the evolution of the filariae and the development of elephantiasis. Now, such an antagonism would be curious since it would mean that, among a whole population of carriers of microfilariae, only those suffering from elephantiasis had any natural immunity against filariae : or (iii) that a large percentage of sufferers from elephantiasis have acquired over a long period an active sterilizing immunity : this prevents the evolution of millions of infective larvae by which they are inoculated in the highly endemic areas where 25–30 per cent. of vector mosquitoes are infected.

However, from all the epidemiological observations of *W. bancrofti*, we can conclude with certainty that elephantiasis is due to this filaria, the geographical distribution being the same. The association of bacteria for the production of elephantiasis is unnecessary.

All the research concerning *W. malayi* shows a striking parallel between the incidence and abundance of microfilariae in a given population and the number of cases of elephantiasis. The aetiological rôle of this filaria is therefore well established.

Recent experience among American troops in the endemic areas in the Pacific indicates that the rôle of " *W. pacifica* " as the cause of elephantiasis, whether it is a separate species or a geographical race of *W. bancrofti*, cannot be doubted.

On the subject of the pathogenesis of the lesions produced by *Onchocerca volvulus*, it is not possible to bring definite evidence as to whether they are caused by mechanical action or a toxin. It is difficult to attribute to the microfilariae of this parasite, which are found in small numbers in the lymphatic glands, any more than one does to those of *W. bancrofti* a rôle of blocking the

blood vessels. On the other hand, if one allows a toxic rôle to this parasite, it is difficult to account for the fact that only a small percentage of cases show lesions ; further, microfilariae may be found in the conjunctiva without causing any interference with vision. One must conclude that either some persons are particularly susceptible, or that some strains of *O. volvulus* are particularly pathogenic.

L. E. Napier

ZANETTI, V. Traitement de certains phénomènes allergiques d'origine filarienne par autoallergène urinaire. [**The Treatment of certain Allergic Phenomena of Filarial Origin with Auto-Allergens from the Urine.**] *Ann. Soc. Belge de Méd. Trop.* 1948, June 30, v. 28, No. 2, 287–92.

Cutaneous allergic manifestations, oedema, pruritus, urticaria and lichenification and thickening of the skin, are mainly associated with *Onchocerca volvulus* infection but may occur with *Loa loa*. They occur mainly in Europeans who have been repeatedly subjected to infection over long periods, and they can be extremely troublesome. The pruritus is sometimes unbearable and interferes with sleep ; this results in violent scratching with subsequent secondary infection.

The author decided to try inoculation by auto-allergens obtained from the urine of the patient. The allergens were prepared by the method of BARBER and ORIEL (*Brit. Encyclopaedia of Med. Pract.*, v. 1, 329).

At first he had doubtful results, but he obtained a very good result in a non-filarial patient allergic to insect bites, with very small doses of allergen. This made him realize that previously he had used too large doses.

He subsequently adopted the technique of giving four test doses into the skin of the anterior surface of the forearm, in strength of 1 in 1,000, 1 in 10,000, 1 in 100,000 and 1 in 1,000,000, sufficient to produce a weal of 2 mm. in diameter. The results were read in 24 to 48 hours : round raised reddish papules of 4 mm. in diameter were produced which disappeared after another day or two. Dilutions of 1 in 100,000 were uniformly positive and 1 in 1,000,000 were doubtful.

The treatment consisted of 10 subcutaneous injections of 0·3 ml. of a 1 in 1,000,000 dilution once a week. Improvement commenced after the first injection and continued. The desensitization usually lasted six months or so, but another injection re-established it. In the pruriginous forms there was sometimes a slight exacerbation after 36 hours preceding the improvement. The author adopted the above dosage as a standard often without preliminary testing : with larger doses there was frequently an oedematous reaction.

L. E. Napier

ALVAREZ CRESPO, J. *Dirofilaria immitis*. Investigación en perros de la ciudad de Guayaquil. [*Dirofilaria immitis*. **Investigation of Dogs in the City of Guayaquil.**] *Rev. Ecuatoriana de Hig. y Med. Trop.* Guayaquil. 1944. Apr., v. 1, No. 2, 199–202, 1 fig. English summary.

HAWKING, F. & SEWELL, P. **The Maintenance of a Filarial Infection** (*Litomosoides carinii*) **for Chemotherapeutic Investigations.** *Brit. J. Pharmacol. & Chemotherapy*. 1948, Dec., v. 3, No. 4, 285–96, 4 figs. on 2 pls. [36 refs.]

Cotton rats naturally infected with the filarial worm *Litomosoides carinii* have been used by CULBERTSON and colleagues in testing possible chemotherapeutic agents in this infection [this *Bulletin*, 1944, v. 41, 772 ; 1945,

v. 42, 136]. Williams and collaborators successfully transmitted *L. carinii* to cotton rats and white rats by the tropical rat mite *Liponyssus bacoti* and described the method of rearing the vector in the laboratory, and also made important observations on the life cycle of the filarial worm *L. carinii* [*ibid.*, 1946, v. 43, 663, 1080 ; 1948, v. 45, 629]. Scott and his colleagues infected cotton rats and white rats with the same filarial parasite through contact of clean animals with cotton rats already infected, and made important observations on the rate of growth and maturity of *L. carinii*. Later that author described the production of quantitative filarial infections in the cotton rat with much technical detail so that accurate chemotherapeutic studies became possible [*Amer. J. Trop. Med.*, 1946, v. 26, 849 ; this *Bulletin*, 1947, v. 44, 447, 839, 840]. In Britain, Bertram and colleagues have also made useful contributions on the same subject [*ibid.*, 1946, v. 43, 1197]. The experiments described by the present authors owe much to the generosity of American workers for demonstrating their methods and providing infective material. Mites were bred on sawdust in jam jars kept in an insectary with a day-old rat or mouse to feed on. The mites were then transmitted in the sawdust to sterile tanks and allowed to feed on infected cotton rats with microfilariae in their blood. Fresh young cotton rats were then introduced to the tanks for the infected mites to feed on after removal of the infected animals. About 8 weeks later, a drop of tail blood was examined, after staining, for the presence of microfilariae. Adult worms are found in the pleural cavity and mediastinum after a time, but may be absent, suggesting that spontaneous cure has occurred. The cotton rat nevertheless appears, from the literature, to be the best experimental animal available. To estimate the value of chemotherapeutic agents, examination of adult worms and microfilariae should be made since various classes of drugs affect the different developmental stages of the worm in different ways. It appeared that six daily doses of drug given intraperitoneally was a suitable method of treatment. Six days after the last dose, the rat was killed and examined for adult forms and microfilariae. The activity of antimonials and arsenicals in this infection, as described by other authors, was confirmed.

J. D. Fulton

Wanson, M. Notes sur le comportement de *S. albivirgulatum* Wanson et Henrard. [**A Note on** *Simulium albivirgulatum* **Wanson and Henrard.**] *Ann. Soc. Belge de Méd. Trop.* 1948, June 30, v. 28, No. 2, 279–85.

Simulium albivirgulatum is widely distributed in the Belgian Congo, coming third in frequency and distribution after *S. damnosum* and *S. griseicollis*. It attacks animals, birds and man. Some notes are given on its habits and a table shows the monthly collections for 1946 and 1947. Numbers are highest for the dry months June to September and lowest in the wet months. This species attacks the lower parts of the body, not usually higher than the knee of a standing man.

At Léopoldville, 0·53 per cent. of captured female *S. albivirgulatum* were found to contain " sausage forms " of *Onchocerca volvulus*. In 6,000 dissections no further development was observed. In the laboratory 362 females were reared and fed on infected volunteers ; a number of these flies were killed, dissected and examined daily for nine days, and the natural findings were confirmed. No larvae of *O. volvulus* were seen in the head or mouthparts and the development in body cavity or thoracic muscles did not proceed beyond the " sausage stage."

H. S. Leeson

See also p. 404, Lewis, **The Simuliidae of the Anglo-Egyptian Sudan.**

Basnuevo, J. G. Tricocefaliasis y arsenicos organicos pentavalentes. [**Trichocephaliasis and Arsenical Compounds.**] *Rev. Kuba Med. Trop. y Parasit.* 1948, Sept.–Oct., v. 4, Nos. 9/10, 185–8.

The English summary appended to the paper is as follows :—

"The author reports on the action of Arsenical compounds on *Trichuris trichiura*.

"Five cases of Trichocephaliasis were treated with Acetylamino-hydroxyphenyl-arsonic-acid mixed with sodium carbonate (Content of a tablet : Arsenic 0·25 Gm., Carbonate 0·15 Gm. Dose : Up to 125 lb., 0·008 Gm. for each pound of weight, for 10 days).

"Administering 4-carbaminophenylarsonic acid also mixed with sodium carbonate (Arsenic 0·25 Gm., Carbonate 0·15 Gm.) the author, treating 14 cases, reports a 64% cure."

Del Carmen Núñez, M. & Mazzotti, L. Incidencia de triquinosis en gatos de la ciudad de Mexico. [**Trichiniasis in Cats in Mexico City.**] *Rev. Inst. Salubridad y Enfermedades Trop.* Mexico. 1948, Mar., v. 9, No. 1, 51–4.

The English summary appended to this paper is published in the *Bulletin of Hygiene*, 1948, v. 23, 956.

Gursch, O. F. **Effects of Digestion and Refrigeration on the Ability of *Trichinella spiralis* to infect Rats.** *J. Parasitology.* 1948, Oct., v. 34, No. 5, 394–5.

The effects of digesting *Trichinella* cysts for periods of 4, 8 and 12 hours in a solution of 1 per cent. pepsin and 0·5 per cent. hydrochloric acid (1 : 80) together with varying periods of refrigeration at 5°C. were tested in relation to the subsequent infectivity of the larvae. One series of 12 rats was fed with 3,000 larvae per rat and a second series of 12 rats with 5,000 larvae per rat. Each rat was killed 24 hours after the infective feed and the larvae recovered from the intestine were counted. The results indicate that the infectivity of the larvae was not impaired by 4 to 8 hours of digestion nor by 24 hours of refrigeration, but 12 hours of digestion resulted in a lowering of the percentage of worms recovered. Larvae exposed to 72 hours of refrigeration, however, showed a much reduced recovery rate, even in combination with only a few hours of digestion.

J. J. C. Buckley

DEFICIENCY DISEASES

Corkill, N. L. **The Poisonous Wild Cluster Yam, *Dioscorea dumetorum* Pax, as a Famine Food in the Anglo-Egyptian Sudan.** *Ann. Trop. Med. & Parasit.* 1948, Dec., v. 42, Nos. 3/4, 278–87, 2 pls. & 1 map. [17 refs.]

"1. Following a locust visitation which destroyed much of the crops in the Fung area of the Sudan in 1938, some 12 wild tubers and roots were widely used as food.

"2. The most important was the cluster yam, *Dioscorea dumetorum* Pax, presumed to contain the alkaloid dioscorine.

"3. Cases of poisoning resulted from its use as a food, although most communities soon evolved methods of detoxication.

"4. The yam was usually prepared either as a cooked whole vegetable, as a flour for making cakes, or as a porridge. Beer was also made from it.

"5. Its nutritive value was mainly as a calorie food, but it also contributed most protein to the famine diet, and seems to have been the main antiscorbutic food, being thus analogous to the potato in parts of Ireland.

"6. Two closely related forms from Asia are referred to."

VELEZ BOZA, F. La alimentación y la nutrición en Venezuela. [**Food and Nutrition in Venezuela.**] *Rev. Sanidad y Asistencia Social.* Caracas. 1948, Jan.–Apr., v. 13, Nos. 1/2, 1–183, 22 pls., 8 charts & 2 maps. English summary.

KOENIGSFELD, E. G. H. & DESAI, V. G. **Corneal Opacities among Children of a Railway Colony in the Dekkan.** *Indian Med. Gaz.* 1948, Aug., v. 83, No. 8, 383–7.

Corneal opacities, affecting one or both eyes, were found in 20 (2·6 per cent.) of 761 children examined. Fifteen of the twenty cases showed wasting and anaemia. No other signs of nutrition deficiency are recorded. Evidence of trachoma was present in only a small number of cases.

The authors conclude that malnutrition is the main aetiological factor, but are unable to incriminate any specific factors. *Dean A. Smith*

RAMALINGASWAMI, V. **Nutritional Diarrhoea due to Vitamin A Deficiency.** *Indian J. Med. Sci.* 1948, Nov., v. 2, No. 11, 665–74. [26 refs.]

It is well known, particularly from animal experiments, that keratinizing metaplasia associated with vitamin A deficiency affects many epithelial structures. While ocular and dermal lesions have received much attention, diarrhoea as a manifestation of human vitamin A deficiency has seldom been recorded.

Twenty children with keratomalacia or Bitots' spots, skin changes, low plasma vitamin A levels and diarrhoea were treated with vitamin A concentrate. The diarrhoea was controlled within 48 hours on this treatment alone and as there was no evidence of infection nor of other nutritional deficiency (except possibly protein) it is concluded that the diarrhoea was part of the avitaminosis A syndrome. *Dean A. Smith*

HAMMOUDA, M. & NAGI, M. **The Use of Pyridoxine in the Treatment of Egyptian Pellagrins.** *Acta Tropica.* Basle. 1948, v. 5, No. 4, 357–9, 1 fig.

Loss of muscular power is frequently found in pellagrins and, unlike the classical features of the pellagrin symptom complex, dermatitis and diarrhoea, is not greatly improved by treatment with nicotinic acid.

Seven pellagrins were tested, before and during treatment, by means of a spring ergometer and it was found that pyridoxine (vitamin B_6) in doses of 50 mgm. daily, by the intravenous route, rapidly restored muscular power. [Several clinical signs such as angular stomatitis, once thought to be essential parts of the pellagra syndrome, are now known to be due to a commonly associated deficiency—in the instance quoted, ariboflavinosis. The present evidence suggests that loss of muscular power may come to be regarded in the same way, as due to an associated pyridoxine deficiency.] *Dean A. Smith*

TROWELL, H. C. **Medical Examination of 500 African Railway Workers.** *East African Med. J.* 1948, Nov., v. 25, No. 11, 423–32. [29 refs.]

The author points out that in many nutritional surveys only clinical Material is collected, there is usually no reference to pathological studies, and this may lead to serious mistakes.

The frequency and incidence of liver disease (especially cirrhosis), of chronic nephritis and of chronic pancreatitis are discussed. DAVIES [this *Bulletin*, 1947, v. 44, 1098] in a review of nearly 3,000 autopsies at Kampala, Uganda, 1,000 livers being examined by himself, considers that these lesions can be traced back to an acute attack of severe malnutrition (kwashiorkor) in childhood. The present author thinks that there is clinical support for the view that malnutrition at this age may lead to certain permanent and incurable defects, while the chronic inflammation of liver and pancreas is apt to lead to carcinoma. This work, however, requires to be extended and confirmed, as the real point at issue is whether these chronic lesions are really the result of malnutrition. There has been no detailed study of the enlargement of the parotids, which, clinically, appears to be part of the syndrome. The cause of the acute lesion is still unknown, and it is uncertain if this begins in the liver, or, as DAVIES suggests [this *Bulletin*, 1948, v. 45, 633] in the pancreas.

Judged by physique and strength of the dynamometer pull, a large proportion of Africans come within the normal range seen in Europeans, but a fair number fall below the standards set by other members of their own tribe, and it is thought that the available evidence suggests that the latter groups represent the effects of disease and malnutrition rather than a normal variability. At autopsy, a large proportion show abnormalities of the liver, pancreas, and salivary and ductless glands. Clinically a number show such signs as soft, brown hair, cracked skin, enlarged parotids, gynaecomastia and enlarged livers. Many of these signs appear to have originated in an acute attack of malnutrition in childhood, but it is considered that more exact tests of renal, pancreatic, and hepatic function must be devised.

On the whole, ordinary diseases were uncommon among railway workers, although the evidence suggests a high incidence of respiratory infections, probably due to overcrowding in the quarters, such infections being the commonest cause of death and absence from work. It is thought that vitamin deficiency did not materially reduce efficiency. The signs of malnutrition as detected in the African soldier (KEKWICK, 1947, unpublished data) and in the railway worker do not suggest any recognized vitamin deficiency, but rather that malignant malnutrition had persisted. This was supported by pathological studies, and explains why many of the signs did not improve on the generous army diet.

The author considers that in certain districts of Africa a fair proportion of the population suffer from varying degrees of malignant malnutrition, have a disease which is progressive and incurable, and can never give efficient work even on a perfect diet. Further, their descendants will be small and nutritionally handicapped, while there can be little progress until the cause and course of this condition is recognized.

[Is malignant malnutrition the main cause of the small birthrate found in many parts of Africa ?] *C. F. Shelton*

SALCEDO, J., Jr., CARRASCO, E. O., JOSE, F. R. & VALENZUELA, R. C. **Studies on Beriberi in an Endemic Sub-Tropical Area.** *J. Nutrition*. 1948, Nov. 10, v. 36, No. 5, 561–77. [23 refs.]

Beriberi ranks second only to pulmonary tuberculosis as a cause of death in the Philippines, having claimed over 24,000 lives in 1947 with a mortality rate of 132 per 100,000. Highly milled rice is the staple.

An attempt is projected to reduce the beriberi incidence in an area of high endemicity by artificial enrichment of the entire rice supply. This paper records the findings of a preparatory clinical survey. In all, 12,384 persons were examined, among whom 1,580 cases of beriberi were encountered.

No significant difference in the incidence of beriberi between the urban and rural populations was found. The individuals were grouped by age and physiological state. The group incidence, in descending order of frequency, was "expectant mothers", "nursing mothers", "other adults", "infants" (0–2 years) and "children" (2–15 years). Although there was a relatively low incidence in infants, mortality in this group was extremely high.

Estimations of thiamin were carried out in a one-hour urinary excretion after a 12-hour fast. The mean excretion in beriberi subjects was somewhat lower than in 65 apparently normal subjects, but there was no correlation between "fasting hour" thiamin excretion and severity of clinical manifestations.

The dietary records of all the individuals surveyed were kept for a nine-day period. The majority of the beriberi cases fell into the groups showing low dietary thiamin calorie ratios. Investigation showed that 15 per cent. of the subjects washed their rice 4 times before cooking, 55 per cent. 3 times and 30 per cent. twice ; all rice washings were discarded by over 80 per cent. of the subjects.

The survey will be repeated after a trial period ; enriched rice will be used.

Dean A. Smith

SPRUE

Suarez, R. M., Perez-Santiago, E., Rodriguez-Molina, R., Torregrosa, M. V. & Benitez-Gautier, C. **Response of Tropical Sprue to Synthetic Pteroyltriglutamic Acid (Teropterin).** *Bol. Asoc. Med. de Puerto Rico.* 1948, Sept., v. 40, No. 9, 235–40.

Five sprue patients in Porto Rico were treated with Teropterin (pteroyltriglutamic acid). Four received 10 mgm. intramuscularly and one 20 mgm. daily, and all five responded in a clinical and haematological sense. The reticulocyte response was maximal even in one who was 88 years of age. One whose sprue was complicated with severe schistosomiasis and pronounced splenomegaly showed definite clinical and haematological response to a daily dose of 20 mgm. No deleterious effects which could be attributed to the triglutamate were observed. A daily dose of 10 mgm. Teropterin which is equivalent to 6·3 mgm. of folic acid, intramuscularly, is probably adequate in the treatment of sprue.

P. Manson-Bahr

i. Suarez, R. M. & Spies, T. D. **The Effectiveness of Vitamin B_{12} in the Treatment of Tropical Sprue.** *Bol. Asoc. Med. de Puerto Rico.* 1948, Aug., v. 40, No. 8, 199–209. [11 refs.]

ii. Spies, T. D. & Suarez, R. M. **Response of Tropical Sprue to Vitamin B_{12}.** *Blood.* 1948, Nov., v. 3, No. 11, 1213–20, 5 figs.

i. Six patients in Porto Rico suffering from tropical sprue were treated with intramuscular injections of vitamin B_{12}. In the first, a single injection of 10 mgm. was given ; in the second a second injection of 20 mgm. was administered seventeen days later and a third of 25 mgm. twenty-six days later. In case 3, a similar dosage was employed. The 4th patient received a single dose of 20 mgm., the 5th one of 4 mgm. and the 6th two 25 mgm. doses at twenty days apart. One patient did not respond to a single dose of 10 mgm. and one other who received 4 mgm. showed only a minimal reticulocyte response.

These responses were much greater when supplemented with folic acid or with liver.

No definite conclusions as to dosage or spacing were arrived at.

ii. This paper appears to refer to five of the patients discussed above.

P. Manson-Bahr

HAMID, A. **Cases of Sprue treated by Laparotomy.** *Indian Med. Gaz.* 1948, Aug., v. 83, No. 8, 374–5.

The underlying idea of performing laparotomy was to observe the effect of localized peritonitis acting as a counter-irritant. As the cases were typical, no stool or blood examinations were done. They were not improving on the orthodox treatments, but the effect of operation was dramatic. The diarrhoea ceased and the patients did not have any motions for three or four days, nor did they develop tympanites.

The laparotomy was performed by a lower median incision, the intestines were gently massaged and a drachm of ether was poured in before the abdomen was closed. No relapses have so far been reported. In each case the illness had persisted for five months to one year. Two cases were in women of 23 and 25 and two were in men of 30 and 40 years respectively. *P. Manson-Bahr*

HAEMATOLOGY

BARNES, G. T. **An Investigation into the Causes of Severe Anaemia in Fiji.** *J. Trop. Med. & Hyg.* 1948, July, v. 51, No. 7, 133–9, 6 figs.

Forty-nine cases of severe anaemia are discussed in this report. Of these 28 (57 per cent.) were in Indian women and 18 (37 per cent.) in Indian males. Only a very occasional Fijian case was encountered.

Twenty could be classified as hookworm anaemia of a hypochromic type which responded satisfactorily to iron. Four of the patients fell into the group " very light " and " light " infestations which may be of no clinical importance. That anaemia-producing factors other than hookworm infestation exist is shown by the absence of correlation between the degree of anaemia and the intensity of infestation. Thus 41 worms were recovered from a patient with a haemoglobin percentage of 31, and 506 from another with haemoglobin percentage of 58.

Furthermore, gastric analysis revealed achlorhydria in one and hypochlorhydria in seven others, suggesting that a deficiency of dietetic iron may be the predisposing cause of the anaemia. Other anaemia-producing factors were malaria in one, and chronic blood loss from haemorrhoids in another. Both these conditions were considered of less importance than hookworm infestation and dietetic iron deficiency.

Among the males, there was a single case of hypochromic anaemia not attributable to hookworms.

It has long been appreciated in Fiji that there exists a special incidence of severe anaemia among young Indian women. These are often seen with a haemoglobin percentage of 20. Fijian women have a lower " normal " level of haemoglobin than the men and it is reasonable to assume that the explanation lies in the iron-deficiency of the Indian diet, inadequate to offset the loss of iron by menstruation and parturition.

Of eleven Indian women tested, five had hypochlorhydria and four others achlorhydria and only two gave gastric analysis curves within normal limits. The ages of the fifteen patients in this hypochromic group ranged with one

exception from 15 to 30 whereas idiopathic hypochromic anaemia in temperate climates is a disease of the fourth and fifth decades. Hookworm ova were found in the stools of ten out of these fifteen. Ankylostomiasis however could be assessed as a contributory cause, the obstetric factor being predominant. Probably the label hypochromic (obstetric anaemia) is most satisfactory.

Four cases of hyperchromic anaemia were seen in Indian women between the ages of 20 to 30. Each had been in childbirth a month or less before admission and showed in this respect a resemblance to hypochromic (obstetric) anaemias. Clinically, in the degree of enlargement of liver or spleen, in the presence or absence of glossitis, there was nothing to distinguish the hyperchromic from the hypochromic patients. The most important feature in the initial stages is the finding of erythroblasts in blood smears and an abnormally high indirect Van den Bergh reaction. This disease is the tropical nutritional anaemia commonly affecting young native women in India.

Dimorphic (obstetric) anaemia was found in six Indian females between the ages of 19 to 30 and in one Indian man. It appears that pregnancy, childbirth and lactation also play a large part in precipitating this severe anaemia. Diagnosis is suggested by finding a remarkable mixture of macrocytes and microcytes in blood smears, but the final verdict is determined therapeutically by combined liver and iron.

Two cases were classified as hypoplastic anaemia; an Indian woman of 25 and an Indian male of 60. The anaemia was very severe in both, the haemoglobin being under 25 per cent. and the red blood corpuscles under 1 million per cmm.; the mean corpuscular volumes were 70 cm. and 80 cm. and colour indices less than unity.

The outstanding feature was their resistance to treatment with full courses of liver, iron, blood transfusions and hydrochloric acid. *P. Manson-Bahr*

SUNDARAM, S. K. **Folic Acid in Megalocytic Anaemias (with a Digression on Achylia Gastrica in Addisonian Pernicious Anaemia).** *Indian J. Med. Sci.* 1948, Nov., v. 2, No. 11, 680–86. [13 refs.]

A series of 14 cases of megalocytic anaemia, some of them complicated with diarrhoea. One was an undoubted case of sprue. All were treated with a preparation of folic acid and a combination of folic acid and liver. With the exception of two cases the results were uniformly good. In some a soluble preparation was used for injection in doses of 1 to 5 cc.: anaphylactic reaction had to be avoided. No therapeutic differences could be found between pure folic acid or folic acid combined with liver. *P. Manson-Bahr*

VENOMS AND ANTIVENENES

BOQUET, P. & LEHOULT, Y. Les méthodes actuelles de préparation et de titrage des sérums antivenimeux. [**Methods Used for the Preparation and Titration of Antivenin**] *Rev. d'Immunologie.* 1948, v. 12, Nos. 3/4, 116–26, 2 figs. [32 refs.]

The development of the methods for preparing antivenene for therapeutic use is briefly reviewed. The early preparations were made by Calmette by the injection of gradually increasing quantities of venom, and antivenene of low potency was obtained, but only after a long series of injections. With the substitution of formolized venom a much more potent antivenene was obtained in a few weeks: the effect of the route of injection of antigen, the interval

between injections and the addition of tapioca, calcium chloride and similar substances was studied ; and the methods of immunization devised to economize antigen in wartime are described. The antibody is associated with the globulin fraction of the serum proteins, can be concentrated by ammonium sulphate precipitation and refined by enzyme digestion.

The methods of testing the potency of antivenene are also reviewed. The authors consider that Calmette's original method, whereby mixtures of varying quantities of antivenene with a constant quantity of venom are injected, gives quickly and easily an estimate of therapeutic value, but it is laborious. Ipsen's method, which has been used with success by other workers, was used by the authors who obtained consistent results on the whole in rabbits and mice ; they emphasize the need for using mice of the same weight and maintained under the same conditions of temperature, diet, etc., during the tests. The limitations of Ipsen's method are pointed out, as well as those of *in vitro* methods based on flocculation.

P. Hartley

Donoso Barros, R. Primeros casos de escorpionismo por *Brachistosternus ehrenbergi* (Gervais) 1841. [**First Cases of Scorpionism by** *Brachistosternus ehrenbergi* **(Gervais) 1841**] *Rev. Med. Chile.* 1948, May, v. **76**, No. 5, 279–81, 1 fig.

The following is a translation of the author's summary.

For the first time there are recorded two cases of scorpionism by the scorpion *Brachistosternus ehrenbergi* (Gervais). Both followed a benign course : however, in one case various manifestations of classical scorpionism were present.

H. J. O'D. Burke-Gaffney

Greer, W. E. R. **Arachnidism. Effect of Calcium Gluconate in Six Cases.** *New England J. of Med.* 1949, Jan. 6, v. 240, No. 1, 5–8. [20 refs.]

" Arachnidism, a definite clinical entity in medicine, is reviewed, and 6 cases successfully treated with intravenous injection of calcium gluconate are discussed.

" Arachnidism should be considered in indigenous areas in the differential diagnosis of the acute surgical abdomen. It may simulate appendicitis, perforated viscus, peritonitis or any other acute surgical emergency.

" The syndrome following the bite of *Latrodectus mactans* may give symptoms referable to many systems of the body. Nervous, cardiac, renal, pulmonary and cutaneous manifestations may be present.

" Burning of the soles of the feet may be pathognomonic in arachnidism.

" One should be familiar with the clinical picture so that proper diagnosis is made and proper therapy instituted with avoidance of unnecessary surgical operations."

DERMATOLOGY AND FUNGUS DISEASES

Nuñez Andrade, R. Trombidiasis por *Neoschoengastia nuñezi* Hoffmann, 1944. [**Trombidiasis caused by** *Neoschoengastia nuñezi* **Hoffmann, 1944.**] *Gac. Med. de Mexico.* 1947, Aug. & Oct., v. 77, Nos. 4/5, 221–44, 31 figs. on pls. [61 refs.] English summary.

In September, 1944, the author observed 6 cases of dermatitis in a family of 3 adults and 3 children in Mexico City. The parasite concerned was *Neoschoengastia nuñezi*, larvae of which were found on the scalp of a girl of three : the disease then spread to the other members of the family.

The disease can affect any part of the skin but attacks particularly the scalp, neck, back, shoulders, axillae and retro-auricular folds. The dermatitis is polymorphic and its forms include petechiae, hives, papules, vesicles and especially molluscoid elements. The prominent feature is itching, together with a burning sensation and constitutional symptoms : leucocytosis and eosinophilia occur. Differential diagnosis from many other skin conditions is required and this is discussed in some detail. The acute stage lasts for one to four weeks. The course is usually benign. Abscesses and moniliasis may occur as complications. The larvae are parasitic on hens and infection is therefore commoner in rural areas : prevention consists of treating chicken-pens with DDT.

The condition responded rapidly to treatment with preparations having a benzyl benzoate base.

The monograph is illustrated with 4 sketches of the larvae and 27 photographs, illustrating the clinical condition and several other forms of dermatitis.

H. J. O'D. Burke-Gaffney

Latapi, F. Carate o mal del Pinto. Clínica y diagnóstico diferencial. Comentario al trabajo del Dr. A. L. Briceño Rossi. [**Differential Diagnosis of Pinta. A Comment on the Views of Dr. Briceño Rossi.**] *Medicina.* Mexico. 1948, Feb. 10, v. 28, No. 549, 58–66.

The chief interest of this contribution lies in the discussion of Briceño Rossi's view that Cuban pinta is not the same as Mexican pinta. It appears that Rossi regards what has been called pinta or Mal del Pinto in Cuba as really a late manifestation of yaws or syphilis. León y Blanco maintains that the Cuban and the Mexican pinta are one and the same, because experimental inoculation of treponemata taken from these produces lesions indistinguishable from one another, and it is suggested that the early manifestations as seen in Mexico have passed unrecognized in Cuba. It is true that in 1944 material taken from a patient with pinta in Cuba, when inoculated into a human subject, produced syphilis, but that is explained by saying that the man suffered also from syphilis. León y Blanco has had the opportunity of studying the disease in both countries and is firmly of the opinion that they are identical. [Further study is needed to set all doubt at rest ; it should be quite possible to inoculate a Mexican pinta subject with material from a Cuban patient and *vice versa* without the risk of inoculating syphilis at the same time. For previous observations by Briceño Rossi, see this *Bulletin*, 1944, v. 41, 866, 867.] *H. Harold Scott*

Duncan, J. T. **The Epidemiology of Fungus Diseases.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1948, Nov., v. 42, No. 3, 207–16. [21 refs.]

In support of his thesis that a survey of fungus diseases in the British tropical colonies is long overdue, the author succinctly reviews with pertinent examples the results of recent studies in other parts of the world on the epidemiology of the dermatomycoses and the systemic mycoses. The need for providing special training in medical mycology and mycological methods for bacteriologists and pathologists stationed in the tropics is emphasized and the suggestion made that one way of meeting this need would be to include medical mycology as an elective subject in the curriculum for the Diploma of Tropical Medicine. *G. C. Ainsworth*

Dowding, Eleanor S. **The Spores of *Histoplasma*.** *Canadian J. Res.* Sect. E. Med. Sci. 1948, Oct., v. 26, No. 5, 265–73, 2 figs. & 4 pls. [14 refs.]

The characteristic, terminally attached, spherical chlamydospores of the mycelial form of *Histoplasma capsulatum*, bear, on all parts of their surface,

tubercles sometimes prolonged into finger-like processes. These structures have been regarded, in the past, merely as projections of the outer wall of the spore. Dr. Dowding, however, has observed that the contents of the projection are continuous, through a narrow channel, with those of the chlamydospore, and furthermore that the whole tubercle or its distal portion may become cut off from the parent chlamydospore by a cross wall and then assume a spherical, oval or pyriform shape, eventually being liberated as a free conidium ; a unique example of a chlamydospore giving rise to secondary conidia. This very important observation, which has a vital bearing on the determination of the systematic position of *Histoplasma capsulatum*, requires independent confirmation. In conclusion, Dr. Dowding refers to earlier suggestions of a probable relationship between *Histoplasma capsulatum*, *Blastomyces dermatitidis* and *Paracoccidioides brasiliensis*. *J. T. Duncan*

Campbell, Charlotte C. & Saslaw, S. With the assistance of Shirley A. Knibb. **The Use of Yeast Phase Antigens in a Complement Fixation Test for Histoplasmosis. II. Results with Ground Antigens.** *J. Lab. & Clin. Med.* 1948, Oct., v. 33, No. 10. 1207–11.

In a previous paper, Saslaw and Campbell [this *Bulletin*, 1949, v. 46, 83], described a form of complement-fixation test, in which antigen suspensions of the intact yeast forms of *Histoplasma capsulatum* and *Blastomyces dermatitidis* were used. The present paper deals with an improved technique for the same kind of test. The antigens were prepared from 5-days-old cultures of the yeast forms of the fungi, which were washed off in sterile buffered saline. filtered through gauze, centrifuged and then re-suspended in buffered saline containing 1 : 10,000 merthiolate to kill the organisms. After 3 to 7 days' storage at 37°C. the merthiolate-killed suspensions were centrifuged and the deposit collected and ground up with small quantities of buffered saline for 30 minutes. The ground-up material was then centrifuged at 3,000 r.p.m. until a clear, cell-free supernatant was obtained, and this supernatant, suitably diluted with buffered saline and preserved with 1 : 10,000 merthiolate, constituted the antigen. Complement-fixation tests with the sera of immunized rabbits, showed that strong cross-reactions occurred when the *Histoplasma* and *Blastomyces* antigens were tested with the homologous and the heterologous antisera, but reactions did not occur when these antigens were tested with normal rabbit serum or antisera for *P. brasiliensis*, *S. schencki* or *C. albicans*.

The common antigenic factor for *Histoplasma* and *Blastomyces* varies in amount with different strains of the organisms, and the authors advise that in diagnostic complement-fixation tests for histoplasmosis, the antigens of both organisms should be used.

As compared with the whole yeast cell type of antigen, the ground-up, soluble extract was more stable in cold storage and did not develop increased anti-complementary properties, and in the tests it gave sharper end-point readings. [See also this *Bulletin*, 1948, v. 45, 644.] *J. T. Duncan*

Dublin, W. B., Culbertson, C. G. & Friedman, H. P. **Histoplasmosis.** *Amer. Rev. Tuberculosis.* 1948, Nov., v. 58, No. 5, 562–70, 11 figs.

" 1. A case of generalized histoplasmosis is reported in which the diagnosis was made by biopsy of a cervical lymph node.

" 2. The organism grew from the buffy layer of the blood after 5·0 cc. of citrated blood were allowed to stand for two weeks at room temperature.

"3. Complement fixation tests using ground mycelial and also filtrate antigens were negative. (Since the tests were made on this patient, positive results of complement fixation tests have been reported in similar cases.

"4. The significance of histoplasmin tests is discussed."

JOHNSON, D. W. & DERRICK, E. H. **Histoplasmosis : Report of an Australian Case.** *Med. J. Australia.* 1948, Oct. 30, v. 2, No. 18, 518–19, 2 figs. (1 on pl.)

In addition to being the first recorded instance of histoplasmosis in Australia, this case presented an interesting clinical history. The only lesion found was a papule measuring 5 mm. in diameter and raised about 2 mm. above the surface of the surrounding skin, situated on the left side of the chin. Clinically this lesion, which was of three months' duration, resembled a basal-cell epithelioma, and it had not broken down nor ulcerated. It was removed by surgical excision and four years later there had been no sign of recurrence. Histologically, the lesion consisted of a granuloma of large monocytes, fibroblasts, various leucocytes plasma cells and some foreign body giant cells. The macrophages in the central part were filled with a parasite resembling *Histoplasma capsulatum*, measuring 3·0 to 4·0 μ in diameter with occasional forms reaching up to 8·0 μ. Unfortunately a culture of the fungus was not obtained, but there is little reason to question the diagnosis of histoplasmosis. *J. T. Duncan*

LACAZ, C. da S., DE FARIA, J. L. & MOURA, R. A. de A. Blastomicose sul-americana associada à moléstia de Hodgkin. (Considerações anátomo-clinicas sôbre um caso.) [**South American Blastomycosis associated with Hodgkin's Disease.**] *Hospital.* Rio de Janeiro. 1948, Sept., v. 34, No. 3, 313–26, 10 figs. [10 refs.] English summary.

Report of a case.

TROPICAL ULCER

CASTELLANI, A. **Some Remarks on the Common Ulcers of the Leg in the Tropics and Subtropics with a Description of Tropicaloid Ulcer (Mycetoid Desert Sore).** *J. Trop. Med. & Hyg.* 1948, Dec., v. 51, No. 12, 245–54, 9 figs.

The author discusses the following :—

True tropical ulcer.—This has many synonyms and is common in the tropics all over the world, its incidence gradually decreasing as the temperate zones are reached. Detailed descriptions are found in all textbooks of tropical medicine, but mention is made of the theory that the condition is of avitaminic and not parasitic origin and that in countries where yaws is common the ulcer may often become infected with the organism of this disease, the patient developing a generalized eruption. Despite the many claims made for specific methods of cure the author regards treatment as very unsatisfactory, recommending rest, local baths with 1 in 2,000 potassium permanganate, and application of 5 per cent. protargol ointment when the ulcer is clean. In some cases the following lotion has been found useful: iodoform ℥i, carbo ligni ℥i, tinct, benzoin ℥i, aether ad℥ vi. Penicillin has not been found to give any striking results [but see this *Bulletin*, 1948, v. 45, 1032].

Veldt sore (diphtheritic desert sore).—This term should be confined to ulcers of diphtheritic origin, the diagnosis being made bacteriologically, and the condition treated with anti-diphtheritic serum administered by injection and applied locally.

Septic ulcer (pyogenic ulcer).—The author considers that this term should be limited to ulcers due to the pyogenic cocci, usually the streptococcus and seldom the staphylococcus. The ulcer often begins as a small pustule or group of pustules, or as a bulla containing pus, which soon bursts. Clinically the appearance is not characteristic, and diagnosis is made on the finding of pyogenic cocci and absence of *C. diphtheriae* and " *Micrococcus* (*Coccobacillus*) *mycetoides* " [surely there are other organisms which should be taken into account ?]. Treatment is by sulphonamides locally and orally, and penicillin locally and by injection.

Tropicaloid ulcer (mycetoid desert sore).—An ulcer commencing usually as a vesicle, which rapidly enlarges and bursts ; the condition is common in many parts of Africa and is often confused with true tropical ulcer or veldt sore. The pathology and bacteriology are very fully described and for full details the reader must be referred to the original paper. A Gram-negative coccus or cocco-bacillus (named by the author *Micrococcus* (*Coccobacillus*) *mycetoides*) is constantly found in initial lesions, the organsim growing well on 1 per cent. trypsin agar and especially on 2 per cent. glucose agar. It can be subcultured and the condition reproduced in human beings by application of cultures to scarified or abrased areas (performed in 13 cases) ; the ulcer is auto-inoculable and hetero-inoculable. Attempts to reproduce the conditions with organisms of the associated flora have failed, and natural immunity does not appear to exist.

In a typical established case one to four ulcers are seen ; these may be open or covered with crusts and are usually on the lower two-thirds of the leg. The ulcers are round or oval, rather superficial, rarely more than 4 cm. in diameter, the margins being usually not undergrained. The ulcers are seldom painful, the inguinal glands are not enlarged, and lymphangitis is never noted ; the lesions may occur anywhere on the body.

Clinically, superficial, infiltrated or nodular, ' eczematoid crusty ', and ' general pyodermia ' types are described. The ulcer has a protracted course of 3 to 12 months or longer.

In treatment, sulphonamides and penicillin should be tried, but the latter is too expensive to use in thousands of cases in some parts of the tropics. The patient is kept at rest for a few days and hot boric fomentations are applied twice daily, an ointment of 4 gm. dermatol [not described] and 26 gm. vaseline is then applied daily on a piece of gauze which is lightly bandaged on. Immediately before application it is useful to swab the sore lightly with hydrogen peroxide. The lotion described above applied once daily is often useful. Vaccines of the causal organisms seem to be useful for treatment in some cases.

The slightest abrasion should be immediately painted with tincture of iodine, and long trousers worn instead of shorts if there is much chance of abrasion from shrubs, etc. Vaccines give no protection.

[The terminology of ulcers found in the tropics has become rather confused and misleading. No mention is made of cutaneous leishmaniasis in this paper.]

C. F. Shelton

MISCELLANEOUS DISEASES

Lewis, H. B., Fajans, Ruth S., Esterer, Marie B., Shen, Chao-wen & Oliphant, Margaret. **The Nutritive Value of some Legumes. Lathyrism in the Rat. The Sweet Pea** (*Lathyrus odoratus*), *Lathyrus sativus, Lathyrus cicera* **and some other Species of Lathyrus.** *J. Nutrition.* 1948, Nov. 10, v. 36, No. 5, 537–59, 1 fig. [27 refs.]

The authors, using young white rats, 50–80 gm. in weight, as their experimental animals, have tested the nutritive values and the toxicities of the following 8 species of *Lathyrus* : *L. odoratus, L. savitus, L. cicera, L. hirsutus, L. tingitanus, L. aphaca, L. sphaericus* and *L. sylvestris Wagneri.*

Those rats which were fed with 50 per cent. of the pea-meal of *L. odoratus*—the one most fully described—uniformly showed signs of lathyrism ; incontinence, paralysis of the limbs and spinal curvature coming on after a fortnight on this diet. With older rats, weighing up to 250 gm., the same clinical picture was produced, but the curvature was less marked. In the femur, changes similar to osteomalacia were produced and in the tibia osteoporosis from demineralization. There was haemarthrosis of the knees, strongly reminiscent of Charcot's disease in man. The toxicity was the same even when casein to 25 per cent. was added, or in the presence of good animal protein. This is of interest in disposing of the theory that tryptophane deficiency is an aetiological factor in lathyrism. The addition of powdered liver extract to the diet also failed to protect against the onset of symptoms of lathyrism, nor did liberal amounts of ascorbic acid affect the issue.

The toxic principle is thermostable, resisting 80°C. for 24 hours, and 120° for 6 hours. It can be removed by slow percolation of the meal with 30 per cent. alcohol, or by cold water, but not by ether.

Analogous details are given, but less fully, of the results of feeding the animals with the other 7 species of *Lathyrus*. *L. sylvestris Wagneri* was the most toxic of all. With this, some of the animals showed symptoms of poisoning after only 4 gm. of the legume had been taken ; the animals would refuse the food in 2–3 days and died between the 4th and 10th days. The symptoms also were more severe : there was excitability, convulsive seizures with increased and spasmodic respiration. The attacks could be induced by slight stimulation such as knocking on the cage, or touching with a rod. Older rats showed a similar train of symptoms, but in them the onset was, as a rule, later. The effects in those which survive appear to be permanent and in one instance it is reported that these attacks could be induced some 8 months after the Lathyrus had been withdrawn.

The authors summarize the results of their experiments with the young white rats in the following words :—

" *Lathyrus sativus* and *cicera* showed no toxicity and promoted growth as effectively as did the edible white split pea of commerce. *Lathyrus aphaca* was nontoxic, but was inferior in growth promotion to the other species.

" *Lathyrus hirsutus, tingitanus, sphaericus* and *sylvestris Wagneri* were toxic, and the last three were unacceptable to rats (they are listed in order of increasing toxicity). Of these, *Lathyrus sylvestris Wagneri* was most acutely toxic and appeared to contain a toxic substance which produced marked injury to the nervous system. The toxic material of *L. tingitanus, sphaericus* and *sylvestris Wagneri* could be extracted by 30 per cent. alcohol and the extracted meal was effective in promoting growth.

" With the species less acutely toxic (*L. hirsutus* and *tingitanus*) it was possible to obtain the skeletal changes described as typical of lathyrism."

H. Harold Scott

BEET, E. A. **Pigmentation of the Tongue in African Children.** *East African Med. J.* 1948, Nov., v. 25, No. 11, 433–7.

"It is concluded that pigmentation of the tongue is not of any apparent clinical significance in Lala children.

"It is possible that the incidence of this condition will be found to vary in different groups living under different environmental conditions."

SINHA, S. B. **Two Cases of Tropical Eosinophilia in Tea Estate Practice.** *Indian Med. Gaz.* 1948, Sept., v. 83, No. 9, 420.

VISWANATHAN, R. **Pulmonary Eosinophilosis.** *Quart. J. Med.* (n.s.) 1948, Oct., v. 17, No. 68, 257–70, 2 figs. on pl. [43 refs.]

After reviewing the relevant literature, the author discusses the aetiology and symptomatology of pulmonary eosinophilosis (or tropical eosinophilia). The clinical material was provided by 207 patients, of whom 189 were army personnel on active service in E. Bengal, Assam, and Burma. Predominating symptoms were cough, lassitude, breathlessness on exertion, fever, asthma, heaviness or pain in the chest, haemoptysis and palpitation. Splenic enlargement was found in 36 per cent. of cases.

Characteristic mottling of the lung fields was found on X-ray examination in 51 per cent. of cases, this was sometimes uniformly distributed throughout both lung fields, and sometimes confined to one lung or a part of a lung. The eosinophils were raised above 2,500 per cmm. in 96 per cent. of cases, and above 10,000 per cmm. in 49 per cent. of cases. There was a raised ESR in 75 per cent. of cases, a high-titre cold agglutination in 76 per cent., a positive W.R. in 49 per cent. and a positive Paul Bunnell reaction in 33 per cent. of cases. Microscopical and cultural examinations of both sputum and blood in 17 cases failed to reveal any specific organism, nor were mites found in specimens of sputum from 21 patients, after examination by the method described by CARTER, WEDD and D'ABRERA [this *Bulletin*, 1945, v. 42, 73]. Total and differential white counts made during the course of treatment showed an initial increase in the eosinophils and a subsequent fall. The reduction in the eosinophil count was not so rapid as the amelioration of symptoms, and normal counts were not obtained until a week to a month after the completion of treatment.

Exacerbation of symptoms and an increase in the eosinophil count after an injection of 0·15 gm. of neoarsphenamine were used as diagnostic criteria to distinguish pulmonary eosinophilosis from other conditions causing eosinophilia, particularly asthma.

Routine treatment consisted of one injection of 0·15 gm. neoarsphenamine followed by seven injections of 0·3 gm. at weekly intervals. One patient developed arsenical encephalopathy and died after the second injection of neoarsphenamine. Autopsy revealed multiple dark reddish-brown areas both on the surface and within the tissues of both lungs. These areas varied in size from 0·5 cm. to 2·5 cm. in diameter, and were peribronchial in distribution. Microscopically they consisted of tubercle-like nodules with a group of giant cells in the centre surrounded by a cluster of monocytes.

Pulmonary eosinophilosis was considered by the author to be a distinct clinical entity, probably an infective process due to an unknown arsenic-sensitive organism. *H. T. H. Wilson*

BERRE, L. A propos d'un cas d'élephantiasis nostras. [**A Case of "Elephantiasis Nostras."**] *Rev. Méd. Nav. (Métropole et Outre-Mer)*. Paris. 1948, v. 3, No. 3, 299–305.

A young man, aged 20 years, a cultivator living in a small village in Basses-Pyrenees, who had never before left his native mountains, came to Bordeaux with a diagnosis of elephantiasis-like oedema of the lower limbs.

Two years previously he had had a pleural effusion; a milky fluid was obtained each time this was aspirated. He also had a swelling of the abdomen. A provisional diagnosis of hydatid cyst had been made, but was later abandoned. Soon after this, swelling of the lower limbs developed. Next year the condition was unchanged, but he had a febrile attack associated with arthralgia during which the swelling declined temporarily.

When he was seen by the author, he had massive oedema of the lower limbs, swelling of the abdomen with a little ascites, and a pleural effusion at both bases. The skin of the lower limbs was hard, thickened and indurated, and the movements of the limbs were restricted. The blood count was within normal limits except that there was a constant eosinophilia which varied from 12 to 20 per cent. This last observation suggested a parasitic infection, but no ova, cysts, or parasites were found in his stools, and no microfilaria in the night or day blood on repeated examination. A biopsy of an axillary lymphatic gland showed nothing significant except dilatation of the lymphatic channels.

An attack of pneumonia caused a temporary improvement and this suggested fever therapy; this was carried out with several substances but was without good effect.

The author had used this case as the basis for a discussion on the aetiology of elephantiasis. He discusses the rôle of bacteria, especially the streptococci which he considers the aetiological agent in both "true" elephantiasis and "elephantiasis nostras".

The two points of interest in the case were the fact that the large central lymphatics were first involved and later the skin lymphatics: this he considers a reversal of the usual order. The second was the eosinophilia which is unusual in the absence of any parasitic infection. *L. E. Napier*

MONTALVAN C., J. A. Enfermedades del hombre trasmitidas por insectos y otros artropodos. [**Human Diseases transmitted by Insects and other Arthropods.**] *Rev. Ecuatoriana de Hig. y Med. Trop.* Guayaquil. 1944, Dec., v. 1, No. 4, 388–409.

PROTOZOOLOGY: GENERAL

JACOBY, N. M. & SAGORIN, L. **Human Toxoplasmosis in England. Report of a Case.** *Lancet*. 1948, Dec. 11, 926–8, 2 figs. [30 refs.]

This is the report of a case, showing symptoms of involvement of the nervous system, which suggested a diagnosis of toxoplasmosis.

An infant of four months was admitted to hospital with a history of persistent crying, anorexia and enlargement of the head. The mother, father and three other children were alive and well. No domestic animals were kept but the house was said to be infested with rats. The diagnosis was based on the clinical and serological findings as noted below.

The child was well nourished, but hydrocephalic. No important abnormalities were noted in heart, lungs or abdomen. The eyes were proptosed and showed deviation to the left and nystagmus. The fundi showed extensive chorioretinitis and optic atrophy and vision was probably negligible.

Radiograms of the skull revealed thinning of the calvarium and areas of calcification in the cerebrum. The cerebrospinal fluid obtained by ventricular tap showed no organisms and cultures were negative. Animal inoculation of gastric washings, blood and cerebrospinal fluid caused no infection nor were any toxoplasma bodies found in any material examined.

Antibody neutralization tests were carried out on the infant and mother. The infant gave a dubious reaction, but the serum of the mother neutralized 25 skin-reactive doses.

The disease had not progressed at the time of the report.

The case would appear to have satisfied most of the criteria for diagnosis of toxoplasmosis short of the demonstration of toxoplasma bodies, but it has to be conceded that in very few cases have these been demonstrated during life.

H. E. Shortt

FRENKEL, J. K. **Dermal Hypersensitivity to Toxoplasma Antigens (Toxoplasmins).** *Proc. Soc. Exper. Biol. & Med.* 1948, July–Aug., v. 68, No. 3, 634–9.

Past and, possibly, latent infections with *Toxoplasma* have previously been demonstrated both by *Toxoplasma*-neutralizing antibody and complement fixation tests. Both these methods have drawbacks. Thus, the neutralizing antibodies are unstable unless stored in the frozen state, the reading of the test cannot be done under a week, and results are often equivocal. It is also necessary to maintain a strain of *Toxoplasma* for the tests. In the case of the complement fixation test, the complement-fixing antibodies are evanescent and would appear to indicate a recent infection only.

These facts rendered it desirable to prepare *Toxoplasma* antigens suitable for skin tests, which would eliminate these drawbacks. The first antigen prepared was from *Toxoplasma* grown in the developing chick by inoculation on to the chorioallantoic membrane of 7–9-day-old chick embryos. The culture was harvested after 4 or 5 days, the membranes ground up, diluted with normal saline solution and then frozen and thawed repeatedly. The suspension was centrifuged, the deposit discarded and the supernatant fluid, after addition of a disinfectant, was passed through a Seitz filter. Uninfected membranes similarly treated acted as control antigens.

This antigen was titrated on guineapigs carrying latent infections of *Toxoplasma*. It was found that 0·1 cc. of a 1 in 50 dilution would produce erythema and induration of 30 and 15 mm. in diameter respectively after 24 hours, while in normal control animals erythema of a few millimetres only in diameter was produced. The control antigen produced an erythema of less than 5 mm. in diameter in both normal and immune guineapigs.

In testing this antigen on man, an induration of 15+mm. at the site of the test dose was considered a positive test if the control antigen gave an induration of not more than 4 mm. The reaction took 24 to 48 hours to develop.

The chick embryo antigen was later replaced by hamster and mouse antigens. These were prepared from the sediment of peritoneal exudate of heavily infected animals which had been infected by the peritoneal route. This had the advantage over the chick embryo antigens of being much richer in *Toxoplasma* bodies in proportion to the cells of the host animal and so possessed of greater potency. The heparinized exudate was centrifuged, the supernatant discarded and the deposit resuspended in 10 times its weight of normal saline solution. The suspension was exposed to ultra-violet light to kill the *Toxoplasma* and accidental contaminants and was then frozen and thawed repeatedly to break up the organisms. A 1 in 1,000 dilution in 0·25 per cent. phenol-saline solution was now prepared as the final antigen for use.

For the control antigen ground-up mouse or hamster spleen, treated in a similar manner, was used.

The antigens were tested for non-toxicity and sterility and then potency tests were carried out on guineapigs with latent *Toxoplasma* infections.

In applying the test to human beings, the result was considered positive if there was induration of 10–30 mm. and erythema of 10–50 mm. in diameter after 48 hours. The control should not show more than about 3 mm. diameter of erythema after 48 hours. The antigens prepared by the means described are referred to as *toxoplasmins*.

When skin sensitivity to toxoplasmin is compared with evidence of neutralizing antibodies in patients, there is shown to be a high correlation. In cases where the skin test was positive and the antibody neutralizing test negative, there was sometimes produced subsequently an anamnestic rise in the neutralizing antibody titre.

The simplicity of the toxoplasmin skin test and the early reading of results are said to make this the most useful single aid in the diagnosis of toxoplasmosis, past or latent, where isolation of the organism is not possible.

H. E. Shortt

Ruchman, I. & Johansmann, R. J. **Biological Properties of a Strain of Toxoplasma recovered from a Fatal Case of Congenital Toxoplasmosis.** *Amer. J. Trop. Med.* 1948, Sept., v. 28, No. 5, 687–95, 4 figs. [14 refs.]

A fatal case of toxoplasmosis in an infant is described, from which the causative organism was recovered. [The statement in the first paragraph that where organisms cannot be demonstrated "the final proof must rest on the demonstration of cross-immunity with a known strain of toxoplasma . . ." surely needs some modification as in all parasitic diseases the final proof is demonstration of the causative organism.]

Toxoplasma bodies were seen in brain material and inoculation into laboratory animals was successful. Cross-immunity studies were made between the strain isolated (C.G.) and a highly pathogenic strain (R.H.) from another source. These showed a high degree of cross-immunity between these strains.

The results give further corroboration to the prevalent opinion that probably there is only one strain of *Toxoplasma* involved in the human and animal infections which have been observed.

This case is a proved addition to the small number of cases where, in the human disease, *Toxoplasma* has actually been demonstrated in the tissues.

H. E. Shortt

ENTOMOLOGY AND INSECTICIDES: GENERAL

Wigglesworth, V. B. **The Insect Cuticle.** *Biol. Reviews.* 1948, Oct., v. 23, No. 4, 408–51. [7 pages of refs.]

Walton, G. A. **A Minute Bethylid Wasp of Medical Interest.** *Proc. Roy. Entom. Soc. London.* Ser. A. Gen. Entom. 1948, Dec. 28, v. 23, Pts. 10 12, 98.

In Sierra Leone, West Africa, there is a minute Bethylid wasp *Scleroderma wollastoni* which frequently stings man especially if it is caught between the skin and the clothing. [The Bethylidae are a family of Vespoid Hymenoptera. *Scleroderma* is parasitic on the larvae of beetles, the eggs being laid on the surface of the host. We do not know of any previous record of Bethylids stinging man.] *P. A. Buxton*

DETHIER, V. G. & CHADWICK, L. E. **Rejection Thresholds of the Blowfly for a Series of Aliphatic Alcohols.** Reprinted from *J. General Physiol.* 1947, Jan. 20, v. 30, No. 3, 247–53. [41 refs.]

CHADWICK, L. E. & DETHIER, V. G. **The Relationship between Chemical Structure and the Response of Blowflies to Tarsal Stimulation by Aliphatic Acids.** *Ibid.*, 255–62. [12 refs.]

Using blowfly adults, *Phormia regina*, from which the antennae and labella have been removed so as to eliminate the olfactory receptors, the authors test the stimulative power of certain organic compounds when brought into contact with the taste receptors of the tarsi. The flies, which are suspended by their wings from a waxed rod, respond to tarsal contact with a 0·1 M sugar solution by extending the proboscis, but this response can be prevented by the addition of an organic substance to the sugar solution. That concentration of a graded series of dilutions of the added substance which prevents the proboscis reaction is taken as a measure of the substance's stimulative efficiency, and is referred to as its threshold of rejection. The technique has enabled series of related organic compounds to be tested and their stimulatory efficiency to be compared with their chemical structure and properties.

In the first paper, the authors report studies on fifteen aliphatic alcohols and, in the second paper, on eighteen aliphatic acids and one mineral acid. It is concluded that stimulation by the alcohols and the acids involves surface energy relationships but it is not certain whether their penetration into the receptor cells or accumulation in the cell membranes causes the excitation. The hydrogen ion is the most stimulative component of the acid compounds and it is concluded that the anion, rather than the undissociated acid, is next in importance. Substitutions and other structural alterations to the acid molecule lessened the stimulative power of the anion, but this was counteracted usually by increased dissociation of the acid resulting in increased stimulatory efficiency due to the hydrogen ions.

The technique is recommended as having applications in the development of improved insect repellents and, possibly, for work on insecticides.

D. S. Bertram

HAFEZ, M. **Ecological and Biological Observations on some Coprophagous Sepsidae (Diptera).** *Proc. Roy. Entom. Soc. London.* Ser. A. Gen. Entom. 1948, Dec. 28, v. 23, Pts. 10/12, 99–104, 1 fig. [14 refs.]

The Sepsidae are a family of minute flies, many of which breed in dung. Their biology has been somewhat neglected, perhaps because they have no direct medical importance.

The author records ten species of Sepsidae in Egypt and describes details of the life history. The early stages are preyed upon and greatly reduced in numbers by certain beetles of the families Histeridae and Staphylinidae.

P. A. Buxton

LEWIS, D. J. **The Simuliidae of the Anglo-Egyptian Sudan.** *Trans. Roy. Entom. Soc. London.* 1948, Dec. 15, v. 99, Pt. 14, 475–96, 4 figs. on 1 pl. & 14 maps. [37 refs.]

The author gives an interesting and valuable account of the distribution of the fifteen species of Simuliids known in the Anglo-Egyptian Sudan, the text matter being illustrated by a number of maps which show at a glance the distribution of the separate species. The species recorded are:—*S. adersi*, *S. alcocki* var. *henrardi*, *S. bovis*, *S. cervicornutum*, *S. damnosum*, *S. dentulosum*,

S. griseicollis, *S. impukane*, *S. lepidum*, *S. mcmahoni*, *S. medusaeformis*, *S. nigritarsis*, *S. ruficorne*, *S. unicornutum* and a new species as yet undescribed. Specific descriptions are not included.

Simuliids flourish in the western tributaries of the Upper White Nile, in the main Nile below Khartoum, and in the Upper Blue Nile and Upper Atbara River areas. The lower part of the Nile in the Sudan is heavily infested with Simuliids. This and certain instances of discontinuous distribution of species in isolated hill regions are discussed in relation to the nature of the water courses which probably existed in the Sudan in ancient times.

Some early accounts, dating back to 1822, of travellers' experiences of flies, now known to have been probably *Simulium*, are quoted.

The paper is not only concerned with the distribution of the species; bionomical notes are contained under species and in sections dealing with the topography and species of particular areas.

The two species biting man in the Sudan are *S. damnosum* and *S. griseicollis*; the former is probably the vector of *Onchocerca volvulus* to man in the Sudan [this *Bulletin*, 1948, v. 45, 531]; onchocerciasis is considered to be responsible for blindness in the Bahr el Ghazal Province [this *Bulletin*, 1935, v. 32, 650]. *S. griseicollis* is a serious biting pest in the northern Sudan.

S. damnosum occurs both in the northern and southern Sudan. It has a wider range of breeding places in the Sudan than in Central Africa, being found on mud in rather placid waters with a speed of 2 km./hour, as well as in rapids. Pupae have been collected from mud, rocks, cords of fish-traps, on sedge and other plants; they occurred even at depths of 60 cm. The habits of the adult are as in other countries; it prefers wooded country but has been found biting in barren rocky desert several kilometres from breeding places. The possibility is mentioned that onchocerciasis may spread to areas populated by *S. damnosum* but as yet free of the filarial parasite.

S. griseicollis is distributed mainly in the lower Nile from the Gezira Area southwards. A small outbreak of flies usually occurs about December but the main fly season is about March, there being probably a reduction of breeding in the intervening period owing to the low winter temperature. In summer, the hot dry climate probably kills off large numbers of adults. This species occurs in immense dense swarms consisting of probably many millions of flies and extending from the river over the desert on both sides. The flies do not engorge readily on man but they cause intense annoyance by walking on exposed parts of the body, particularly on the head, and probing the skin. Engorgement on man is slow, taking from 4 to 16 minutes. Birds, domestic poultry, cattle, horses and donkeys are attacked viciously, and there are reports of donkeys, caged birds and poultry dying of mass infestations of the fly. Biting rarely occurs indoors, and ceases after twilight. Both sexes, but particularly the males, are found probing date and mango flowers. They can be seen resting on vegetation during the day but disappear at night. The day-time clouds which are so characteristic of heavy densities of this species may contain both males and females.

Breeding takes place mainly in unbroken river water, the larvae and pupae being found not only on sedge, roots, sticks and stones but—and this is of particular importance—on moderately hard mud in water flowing as slowly as 0·8 km./hour. Dense clusters of pupae occur at depths of 75 cm. and probably deeper. In the Dongola area, on the lower Nile, and severely infested by this species, the Nile is 600 to 1,300 metres wide and even at low water is a large river. Owing to erosion and deposition there is both a constant slow destruction and formation of islands. The banks are also subject to changes in form. There is, therefore, a continual change in the position of the many mud areas suitable for breeding *S. griseicollis*. Breeding in this mud is profuse and probably far

exceeds the amount of breeding which occurs on sedges and other substrata.

The author draws particular attention to the importance of this mud environment. It is considered that earlier records of *S. griseicollis* having flown long distances (including up to 200 miles) probably overlook the fact that the swarms were derived from mass breeding on mud in local and placid waters, and not from distant rapids as was supposed. However, records of flights up to 80 km. from the Nile seem to be true, and the fly is known to occur in the desert near Dongola in numbers sufficient to cause annoyance.

Domestic animals are sometimes provided with protective smoke clouds or dark shelters during the day, or they feed only outdoors at night. Protective smokes and clothing are employed by the human population ; fly areas are avoided in the fly season, or outdoor work is done during windy weather when the fly is less active. The use of repellents is thought to be the most practicable large-scale measure against *S. griseicollis*. Undiluted liquid dimethyl phthalate has given promising results for *S. griseicollis* and *S. damnosum*, flies alighting for only an instant on the treated skin. In view of the dry air and cool temperatures of the fly season it is not thought that sweat is a serious disadvantage to the use of this repellent.

Human agency appears to play little part in the dispersal of *Simulium* spp. in the Sudan ; irrigation schemes have been responsible for the occurrence of Simuliid breeding in some places.

This paper contains much detailed information and should be consulted in the original by those interested in the bionomics of *Simulium* species and the problems arising in their control. *D. S. Bertram*

MACKERRAS, M. Josephine & MACKERRAS, I. M. **Simuliidae (Diptera) from Queensland.** *Australian J. Sci. Res.* Ser. B. 1948, May, v. 1, No. 2, 231–70, 14 text figs. & 4 figs. on 2 pls. [14 refs.]

The authors undertook a survey of the Simuliidae of south Queensland, Australia, during the period February to June 1947 with a view to establishing the identity of the pest species, generally considered to be *Austrosimulium bancrofti* (Tayl.), concerning the morphology of which conflicting statements had appeared.

Prior to this survey, three species had been reported from Queensland but the present paper increases the number to eight species and one subspecies, four of the species and the subspecies being new to science. Keys and figures are given for the identification of adults, pupae, cocoons and larvae, and notes on the biology of the species are appended to the systematic descriptions.

A. bancrofti was found to comprise two species which had hitherto been confused, namely, *A. brancrofti* (Tayl.) and *A. pestilens*, n.sp., the latter being the important biting pest of the inland region of Queensland. *A. bancrofti* (Tayl.) has nine antennal segments and *A. pestilens* ten ; there are other minor differences. The immature stages are more readily distinguished.

The pest species, *A. pestilens*, has a very short season, apparently about March–April chiefly, the fly wave beginning ten days after the flood waters come down and lasting for 10–14 days. Only in the event of repeated floods do further fly waves occur. The larvae and cocoons are found in the torrential (speeds over 4 ft. per second), turbulent, muddy water and are attached particularly to the submerged branches and fronds of the tea-tree *Melaleuca branchiata*. As the flood waters recede, larvae and living pupae are no longer found, but the intensive breeding during the height of the flood is apparent by the exposed masses of empty pupal shells in their cocoons. Adult *A. pestilens* occur in great numbers on the *Melaleuca* shrubs of the stream bed and the river

banks ; they attack man and domestic stock viciously. They have been reported as following stock for ten to twelve miles from the breeding place but, otherwise, do not seem to disperse far from the water-courses.

Larvae of *A. bancrofti*, and of other species, entirely replace *A. pestilens* as the rivers slow down and become less muddy, but despite the large numbers of adults of *A. bancrofti*, and of other species, which must emerge, few or none have been found in the vicinity of the breeding places. Either their habits were cryptic or dispersal was rapid and wide. *A. bancrofti*, although known to bite man and animals, was not troublesome in Queensland.

S. ornatipes Skuse was the only species seen to oviposit and the only species of which the eggs were found. The females did not enter the water but deposited their eggs at the very edge of the water on logs, grass, and rocks. Development from oviposition to adult probably required two to three weeks, the egg and the pupal stage lasting about five and three days respectively.

The subsidence of the floods followed by complete drying up of streams prompts the authors to suggest that there must be a stage, probably the egg, which resists desiccation and enables the inland species, including *A. pestilens*, to pass through the long periods of summer drought to which they are exposed.

In a brief discussion of the control of *A. pestilens*, it is pointed out that the terrain is difficult to traverse by land during the floods, but that the addition of DDT, if necessary from aircraft, to the torrents or the use of DDT-dipped cattle as poison baits, are methods worth a trial. At present, smudge fires are used for the local protection of man and animals.

An apparatus for breeding out larvae and pupae collected in the field is described and figured. *D. S. Bertram*

VÁRGAS, L. & DÍAZ NÁJERA, A. Nota sobre la identificación de los simulidos de Mexico. El subgenero *Mallochianella* n. n. [**A Note on the Identification of Simuliidae in Mexico.**] *Rev. Inst. Salubridad y Enfermedades Trop.* Mexico. 1948, Mar., v. 9, No. 1, 65–74, 2 figs. on pl. [10 refs.]

The English summary appended to the paper is as follows :—

" The authors present a key for the identification of seven genera of Simuliidae giving a new definition of them. Within the genus *Gigantodax* they propose the new name *Mallochianella* for a subgenus with *Simulium* (*Mallochianella*) *sibirica* (Enderlein), 1930, as the subgenus type. According to the new definition of *Gigantodax* its distribution now includes an Australian species ; formerly the genus was considered as neo-tropical. For the first time now appear keys for the identification of the adults of the Mexican blackflies."

HERTIG, M. **A New Genus of Bloodsucking Psychodids from Peru (Diptera : Psychodidae).** Reprinted from *Ann. Entom. Soc. America*. 1948, Mar., v. 41, No. 1, 8–16, 13 figs. (12 on 2 pls.).

Descriptions are given of the female and male of *Warileya phlebotomanica* n. gen. and n. sp. These flies are similar to sandflies of the genus *Phlebotomus* but the new genus is created on account of differences mainly in size, the wing-shape and posture, the cibarium of the female, and in the male genitalia.

During extensive collecting of *P. verrucarum*, *P. noguchi* and *P. pernensis* in connexion with studies on Carrión's disease, small numbers of female *W. phlebotomanica* were taken occasionally in houses, caves, pigpens, and on stone walls. Only six males have been found. They were taken in the vicinity of a stone wall on top of which ran an irrigation channel, an environment where numerous females were collected. Females were captured containing blood [? origin] ; they fed on man in the laboratory and were twice seen to bite man

in nature. They fly with the short, hopping flight of *Phlebotomus*. The majority of the specimens were taken at altitudes between 2,000 and 2,400 metres. This zone is covered by the distribution range of the three species of *Phlebotomus* and is the upper limit for verruga; there is no evidence of any part which *W. phlebotomanica* may play in transmitting the disease. *D. S. Bertram*

VAN DER KUYP, E. **Mosquito Records of the Netherlands Windward Islands.** *Amer. J. Trop. Med.* 1948, Sept., v. 28, No. 5, 747–9.

The Netherlands Windward Islands in the Caribbean sea consist of St. Martin, Saba and St. Eustatius. The population (3,622 in 1946) is diminishing. This short note describes the climatic conditions and gives a list of seven species of mosquitoes collected during a two-week survey in the dry season in April, 1947. The mosquitoes collected were: *Aëdes aegypti*, *Culex quinquefasciatus* [*C. fatigans*] (both common) *Aëdes busckii*, *Culex americanus*, *C. bahamensis*, *C. habilitator* and *Deinocerites cancer*. No anophelines were taken, although special search was made. There is little evidence of mosquito-borne diseases in these islands at the present time. Cases of malaria mentioned in Government reports have always been confined to people who had visited other islands. Of four people found at Curacao infected with *Wuchereria bancrofti*, two at least may have been infected in the Netherlands Windward Islands. Autochthonous cases of dengue have been found but the last two cases of yellow fever were reported on St. Martin in 1879. *H. S. Leeson*

TRAGER, W. **Biotin and Fat-Soluble Materials with Biotin Activity in the Nutrition of Mosquito Larvae.** *J. Biol. Chem.* 1948, Dec., v. 176, No. 3, 1211–23, 1 fig. [30 refs.]

GOLBERG, L. & DE MEILLON, B. **The Nutrition of the Larva of *Aëdes aegypti* Linnaeus. 3. Lipid Requirements.** *Biochem. J.* 1948, v. 43, No. 3, 372–9. [30 refs.]

GOLBERG, L. & DE MEILLON, B. **The Nutrition of the Larva of *Aëdes aegypti* Linnaeus. 4. Protein and Amino-Acid Requirements.** *Biochem. J.* 1948, v. 43, No. 3, 379–87. [43 refs.]

PARKER, A. H. **Stimuli involved in the Attraction of *Aëdes aegypti*, L., to Man.** *Bull. Entom. Res.* 1948, Dec., v. 39, Pt. 3, 387–97, 1 fig.

The author has studied the rôle of warmth, moisture and smell as stimuli attracting female *Aëdes aegypti* to the host.

The apparatus used consisted of a glass tube, 29 cm. long and 5 cm. in diameter. Each end was fitted with a metal cup, 1 cm. deep, inserted base innermost and with netting stretched across a wide hole cut in its base. The tube was mounted in a chamber lined with white paper and illuminated by a diffused overhead light. Holes in this chamber allowed for the introduction of mosquitoes and test objects as well as for observation. The experiments were made in a room at 28±1°C. and 50–70 per cent. relative humidity. It was not practicable to obtain mosquitoes of the same age for each experiment, but the tabular matter records the range of age for each group; they were fed solely on sugar solution.

For each experiment, 30 mosquitoes were lightly anaesthetized with ether and transferred to the tube. When they had recovered, counts were made at each half-minute interval during a five-minute period of the number of mosquitoes on the netting at one end. A test object (*e.g.* the hand) was then placed on the cup of this same end and counts were made as before. The

mosquitoes could not touch the test object. The first count was the "control" and the second the "test" count. This procedure was repeated at least twice for each object.

The author expresses the result as an Index of Attraction (Ia), derived thus:—

$Ia=\frac{100\ T}{T+C}$ where T is the total number of mosquitoes observed on the netting in the presence of a test object, and C is the number observed in the absence of any test object.

An Ia of 100 indicates maximum positive response [attraction], of 50 indifference, and of 0 a maximum negative response [repellence].

Responses were determined for the hand, warmth (water in a flask at the temperature of the palm of the hand and at the palm temperature plus 1 to 4°C.), cold moisture (water-soaked filter paper at room temperature), warmth plus moisture (water-soaked filter paper over the water flask at palm temperature), and cold sweat, representing smell (sweat-soaked filter paper at room temperature).

Warmth alone was found in ten tests to have no marked attractive, nor repulsive, effect (Ia=36·1 to 56·9). The author considers the possibility that activation of the mosquitoes by warmth might have caused them to land on and leave the netting in rapid frequency with the result that the counts made at particular instants would underestimate the actual number of mosquitoes attracted to the netting by the warmth. However, the number of mosquitoes landing on the netting over a period of time in the absence, and in the presence, of warmth was 66 and 69 respectively, and it is concluded that warmth had neither a marked attractive nor activating effect.

The following mean Ia values were obtained from twelve tests of the other test objects: hand (69·6), warmth plus moisture (65·5), cold sweat (73·3), cold moisture (69·1). These results indicated attraction by all four objects but the activating effects induced by them required consideration. In this series, activation was estimated by (*a*) counting the number of mosquitoes leaving the netting in a given period of time, and (*b*) recording the percentage probing at the netting. The numbers leaving the netting were 503 (hand), 576 (warmth plus moisture), 209 (cold sweat), 173 (cold moisture) 13 (no test object), while the percentages probing were 52·9 (hand), 59·3 (warmth plus moisture), 20·3 (cold sweat), and 21·9 (cold moisture). It is concluded that the Indices of Attraction for these test objects are misleading and that, if allowance is made for the activating effect of each stimulus, then the hand and warmth plus moisture are markedly, and possibly equally, attractive and activating but that cold sweat and cold moisture are less stimulating in both respects. Of these, cold sweat appeared to be more attractive than cold moisture. This is presumed to be due to an olfactory stimulus inherent in the sweat. Statistical tests are applied in comparing data not obviously significant at inspection.

In further discussion of the lack of activation and attraction by warmth alone as opposed to the marked activation and attraction of warmth plus moisture it is postulated that response to warmth may take place only under certain conditions of humidity.

The work of DeLong *et al.* (*Rep. Nat. Res. Coun. Insect Contr. Comm.*, Washington, 1945, No. 176), is noted as being in general agreement with the results obtained in the present experiments but it is observed that Christophers [this *Bulletin*, 1948, v. 45, 40] records *Aëdes aegypti* being attracted to warmth (40°C.) and showing little additional attraction to warmth plus moisture and that moisture at room temperature had "no attractive effect." It is suggested by the author that, whereas DeLong's experiments

were made in environmental conditions similar to those of the present study, Christophers worked at 25°C. and 95 per cent. relative humidity with mosquitoes maintained solely on water. These differences, it is suggested, particularly in temperature and humidity, might cause the differences in response to warmth and to moisture which are apparent in comparing the results of Christophers with those in the present paper. *D. S. Bertram*

Brennan, J. M. **New North American Chiggers (Acarina, Trombiculidae).** *J. Parasitology.* 1948, Dec., v. 34, No. 6, 465–78, 14 figs.

Holstein, M. Les sérums précipitants. Fabrication et limitation dans le temps de leur emploi pour la détermination du sang ingéré par les insectes hématophages. [**Preparation and Reduction in the Time of using Precipitin Sera for detecting Ingested Blood in Insects.**] *Acta Tropica.* Basle. 1948, v. 5, No. 4, 306–26. [74 refs.]

The paper gives a good deal of attention to the history of the development of the precipitin reaction and describes several methods of making specific sera. The author has applied them to the study of blood in lice and bed bugs.

He used several methods for preparing specific sera and appears to have developed a novelty in one respect: Two hours before each inoculation of antigen, the rabbit is given an injection of 10 cc. of 10 per cent. glucose in water. It seems that after this procedure, the rabbit may be brought into use nine days after the commencement of its course of three injections.

On testing his sera on the remains of blood in lice and bugs which had been fed on man a positive reaction was obtained in *Pediculus* even up to the twelfth day after feeding. [This appears to imply that the insects could survive for twelve days without further meals, which is indeed remarkable.] In *Cimex*, a positive reaction was obtained as late as 36 days after feeding. When bugs were tested a few days after feeding, positives were obtained even with blood diluted to 1 in 15,000. With both insects the reactions were shown to be specific to human blood, for negative reactions were obtained with anti-horse, anti-cow and other sera. *P. A. Buxton*

Roman, E. & Nalin, P. Invasion d'Ornithodores dans une habitation humaine en Haute-Provence. [**Invasion by Ticks of a Dwelling-House in Haute-Provence.**] *Ann. Parasit. Humaine et Comparée.* 1948, v. 23, Nos. 3/4, 214–19, 2 figs. [17 refs.]

The inhabitants of a farm near Forcalquier (Provence) had occasion to have a stove installed in an upper bedroom which was situated just below a pigeon-house. This necessitated operations on the ceiling, so that there was a communication between the room and the pigeon-house. In the flue of the stove, specimens of *Ornithodorus coniceps* (Can.) were found. This tick is uncommon and is a parasite of pigeons.

A number of persons in the house were bitten at night and the bites resulted in very intense pruritus with extensive oedema.

This is the first time that *O. coniceps* has been recorded in Provence.

H. J. O'D. Burke-Gaffney

Browning, H. C., Fraser, F. C., Shapiro, S. K., Glickman, I. & Dubrûle, M. **The Biological Activity of DDT and related Compounds.** *Canadian J. Res.* Sect. D. Zool. Sci. 1948, Oct., v. 26, No. 5, 282–300. [31 refs.]

Frowning, H. C., Shapiro, S. K. & Dubrûle, M. **The Insecticidal Activity of DDT and related Compounds against Different Insect Species.** *Canadian J. Res.* Sect. D. Zool. Sci. 1948, Oct., v. 26, No. 5, 301–6. [21 refs.]

Schneller, G. H. & Smith, G. B. L. **Unsymmetrical Analogs of DDT.** *J. Amer. Chem. Soc.* 1948, Dec., v. 70, No. 12, 4057–9. [Refs. in footnotes.]

Trapido, H. **The Development of a Sprayer for Use with Water-Suspensions of DDT in Rural Areas of Latin America.** *Amer. J. Trop. Med.* 1948, Sept., v. 28, No. 5, 721–39, 16 figs. on 5 pls.

Sprayers originally designed for use with insecticide emulsions and solutions have been found unsuitable for use with water suspensions of DDT, because, among other things, of the sticking of valves and the plugging of nozzles. In practice, time is wasted in putting these right and the cleaning of nozzles and filters with pins and bits of wire results in damage to these parts and the delivery of erratic sprays. Power-driven sprayers are often impracticable and expensive to operate. Experienced mechanics are not always available to repair the machines and hand labour is often cheaper than motor-operated mechanical equipment. Moreover, some houses cannot be reached with truck-mounted power sprayers. What is required is a durable, simple, one-man, hand-operated, knapsack sprayer, capable of efficiently delivering DDT water suspensions.

This paper gives a full description of the basic unit and of the modifications made to it which overcome these disadvantages. The main alterations are the provision of: a basket-type filter which is easily accessible and replaceable by hand, without the use of tools; a filler cap by-pass which may be rotated to open or close the sprayer, independent of the hose, by-pass or outlet pipe; a pressure release valve of the automobile type which can be used for releasing air pressure when the liquid has been expended and before the filter cap is opened, and by means of which air pressure can be put into the sprayer from a compressor whenever one is available; a second relief valve which is operated by finger pressure and a combined standpipe, funnel and preliminary filter, which is removable and permits filling of the sprayer to a standard level only, avoids wastage of DDT mixture when filling and screens the material as it enters the tank.

As well as describing the modifications the author illustrates his paper with scale drawings of the parts and photographs. *H. S. Leeson*

Parr, H. C. M. & Busvine, J. R. **A Spinning-Disk Sprayer for applying Residual Insecticides.** *Ann. Applied Biol.* 1948, Sept., v. 35, No. 3, 359–68, 5 figs.

Ordinary knapsack sprayers have been found to be very satisfactory for applying residual insecticides to surfaces in dwellings, etc. When using a Kent type sprayer, the fluid is ejected in the form of a rotating hollow cone, which expands, and becomes thinner, forming threads and, finally, droplets. The origin of these droplets in a rotating cone gives them a variety of initial directions, the range of which is determined by their original velocity, depending on the pressure employed, and the size of the droplets. The larger droplets have more momentum relative to their air resistance (surface area) than the small droplets; consequently they tend to travel farther in still air. However, the movement of the cloud of spray droplets soon produces a forward air current which carries along the finer droplets. Therefore, very fine and coarse droplets travel farthest. Spray clouds from 1/16 in. and 1/32 in. nozzles, when water or kerosene were used at different pressures, resulted in the production of droplets which varied considerably in diameter, but whose size mainly lay between 0·1 and 0·4 mm.

By using the spinning-disk apparatus described by the authors, droplets of the same order of size as those from a Kent type sprayer, *i.e.* 0·1–0·4 mm.

diameter, can be produced, and by altering the speed of rotation, uniform droplets of the required size, between these limits, can be consistently produced. The apparatus can be used to coat various surfaces up to 1 ft. square with deposits of insecticides in oil solution or in aqueous suspensions or emulsions, and these deposits can be controlled and estimated with a fair degree of precision. As a result, it is possible to apply a definite and known amount of insecticide to a surface and to repeat such deposits to within 5 per cent. error at the most.

The apparatus is fully described, and those interested should consult the original for details concerning the construction of the sprayer and the methods to be employed when using it. *R. M. Gordon*

BOHART, R. M. **A Comparison of DDT and Dichlorodiphenyl Dichlorethane as Larvicides for *Aëdes* Mosquitoes.** *J. Econom. Entom.* 1948, Oct., v. 41, No. 5, 834–5.

"In laboratory tests with DDT and dichlorodiphenyl dichlorethane in xylene emulsions against *Aëdes* larvae collected in salt marshes of central California, the latter compound was found to be two to three or more times as toxic, depending upon the concentration used. Also, *Aëdes squamiger* was found to be much more resistant to both materials than was *A. dorsalis*. Both of these discoveries may have a practical application since (1) dichlorodiphenyl dichlorethane has been considered as a substitute for DDT where danger of residues to man, domesticated animals and wild life is a factor, and (2) *A. squamiger* or *A. dorsalis* may frequently be found in 'pure culture,' and can be treated with different dosages of larvicide when so found."

GINSBURG, J. M. **Toxicity of Parathion to Mosquitoes.** *J. Econom. Entom.* 1948, Aug., v. 41, No. 4, 649–50.

Parathion, a new insecticide of German origin, is an ester of thiophosphoric acid. It is highly insecticidal [but so dangerous to vertebrates that it is unlikely to come into general use].

The author has tested parathion against *Aëdes aegypti*. Parathion as an emulsion, diluted in water, killed all larvae at a dose of 0·005 of a part per million; used as a dust the same result was obtained with 1/200th lb. per acre. Quantities of DDT, quoted for comparison, are ten times greater for the same kill. Pupae are many times more resistant than larvae to both insecticides.
P. A. Buxton

DAVIES, W. H. & SEXTON, W. A. **Chemical Constitution and Insecticidal Action. I. Organic Sulphur Compounds.** *Biochem. J.* 1948, v. 43, No. 3, 461–7. [15 refs.]

AINLEY, A. D. & SEXTON, W. A. **Chemical Constitution and Insecticidal Action. 2. Substituted α-Aminonitriles.** *Biochem. J.* 1948, v. 43, No. 3, 468–74. [12 refs.]

LABORATORY PROCEDURES

LEIBOVITZ, A. **The Thick Smear Identification of Malaria.** *Bull. U.S. Army Med. Dept.* 1948, Dec., v. 8, No. 12, 956–8.

A rapid method for staining thick drops of blood is described :—

1. Apply eosin stain for 15 seconds. The stain is prepared by adding eosin Y (2 gm.) to a buffer solution of 17 gm. of dihydrogen sodium phosphate, 5·6 gm. of disodium hydrogen phosphate in 1,000 cc. of water.
2. Wash for 15 seconds in distilled water buffered at *p*H 7·2.
3. Apply polychrome methylene blue for 60 seconds. The stain is prepared by placing in a boiling water bath for 1 hour, 2 gm. of certified methylene blue (*not* medicinal), 17 gm. of disodium hydrogen phosphate in 100 cc. of water. Then 5·6 gm. of sodium dihydrogen phosphate, 75 cc. of methyl alcohol and 900 cc. of water are added. The mixture is ripened in the refrigerator for a week.
4. Wash for 60 seconds in distilled water buffered at *p*H 6·0, and then for 5 seconds in water of *p*H 6·8.

The advantage of this stain is stated to be that it brings out Schüffner's dots vividly throughout the thick drop. It does not apparently stain Maurer's dots, so the method would be of little advantage in the numerous areas where the dominant parasites are *P. falciparum* and *P. malariae*.

P. C. C. Garnham

BARBOZA, A. Novo metodo de coloração e montagem de hirudineos, helmintos e pequenos artropodos. [**A New Method for Staining and Mounting Leeches, Helminths and Small Insects.**] *Anais Acad. Brasileira de Ciencias.* 1948, Sept. 30, v. 20, No. 3, 277–80, 3 figs.

REPORTS, SURVEYS AND MISCELLANEOUS PAPERS

KYLE, J. **Health Regulations for Air Travel (II).** *Brit. Med. J.* 1948, Dec. 25, 1115. [Summary appears also in *Bulletin of Hygiene.*]

BARRETT [see *Bulletin of Hygiene*, 1948, v. 23, 80] has recently discussed various aspects of health regulations for air travel including the international Convention for Aerial Navigation 1944, the vaccines which should be injected and their dosage and certain regulations affecting aircraft and crews. He drew attention to the fact that practically all international flights are, from the point of view of quarantine, well within the incubation period of the major epidemic diseases.

Kyle has continued these instructions and gives detailed information concerning the diseases against which immunization must be carried out for those travelling by British Overseas Airways (see table).

Doctors are advised to ensure that their patients are in possession of the international form of certificate recommended by the International Sanitary Convention for Aerial Navigation, 1933, as amended in 1944.

Passenger Protective Requirements for Specific Routes from England and Return, Including Stopping Places on Each Route (Revised November 19th 1948)

	Yellow Fever	Smallpox	Cholera	Typhus	Plague	TAB
No. 1 Line—London-Cairo	—	Yes	R	R	R	R
No. 2 Line—Cairo-London	—	R	R	R	R	R
No. 4 Line—Southampton-Alexandria	—	R	R	R	R	R
Alexandria-Southampton	—	R	R	R	R	R
No. 1 Line—London-Accra	Yes	Yes	R	R	—	R
Accra-London	Yes	Yes	R	R	—	R
No. 1 Line—London-Teheran ...	—	R	R	R	R	R
Teheran-London ...	—	Yes	R	R	R	R
No. 2 Line—London-Johannesburg ...	Yes	Yes	R	R	R	R
Johannesburg-London ...	Yes	Yes	R	R	R	R
No. 2 Line—London-Sydney	R	Yes	Yes	R	R	R
Sydney-London	R	Yes	Yes	R	Yes	R
No. 2 Line—London-Calcutta ...	—	Yes	R	R	R	R
Calcutta-London ...	—	Yes	Yes	R	Yes	R
No. 3 Line—London-						
(*a*) New York ...	(*a*)—	Yes	—	—	—	R
(*b*) Montreal and return	(*b*)—	No	—	—	—	R
No. 4 Line—Southampton-Singapore	R	Yes	Yes	R	Yes	R
Singapore-Southampton	R	Yes	Yes	R	Yes	R
No. 4 Line—Southampton-Iwakuni ...	R	Yes	Yes	R	R	Yes
Iwakuni-Southampton ...	R	Yes	Yes	R	R	R
No. 4 Line—Southampton-Hong Kong	R	Yes	Yes	R	Yes	R
Hong Kong-Southampton	R	Yes	Yes	R	Yes	R
No. 4 Line—Southampton-Sydney ...	R	Yes	Yes	R	Yes	Yes
Sydney-Southampton ...	R	Yes	Yes	R	Yes	Yes
No. 4 Line—Southampton-Bahrein ...	—	Yes	R	R	R	R
Bahrein-Southampton ...	—	Yes	R	R	R	R

" U.S.A. requires passengers from India, Pakistan and Syria to have cholera certificate.

" Japan requires children 1–15 years to be inoculated against diphtheria.

" ' Yes ' indicates that the inoculation or vaccination is an essential requirement without which the passenger will be held in quarantine on arrival or may not be permitted to embark.

" — indicates there is no requirement.

" R indicates that owing to the presence of the disease or other circumstances the inoculation or vaccination is desirable for the passenger but it is not an essential requirement.

" Protective inoculations against major epidemic diseases are required as follows : *Smallpox* : for practically all routes. *Yellow fever* : for journeys to

and from West and South Africa. *Cholera* : for all journeys to and from India and Far East. It is also advisable to be protected if *en route* to West Africa and Egypt. *Typhus* and *typhoid group* (T.A.B.C.) : for these diseases protective inoculation is recommended, though not essential on all routes. *Plague* : for journeys from some airports in the Orient." *F. O. MacCallum*

CONGO BELGE. Rapport sur l'Hygiène Publique au Congo Belge pendant l'année 1947 par le médecin en Chef de Colonie. [**Report on the Public Health in the Belgian Congo during 1947.**] 152 mimeographed pp., 1 folding map and 3 charts.

This publication, like its predecessors [for 1946 Report see this *Bulletin*, 1948, v. 45, 549] contains a wealth of carefully detailed statistical information and commentaries which one has come to expect in the reports of the *Médecin en Chef* of the Belgian Congo. Figures are given for population, demographic distribution, incidence of diseases and deaths and the like over many years—in some cases for as far back as 1928.

So complete and detailed a record does not lend itself readily to abstracting, but it may be stated that the seven chapters are presented on the usual lines, namely, (1) general organization and demography, (2) discussion of pestilential, epidemic, endemic and other diseases, (3) medical provision for the indigenous people, which includes that of the well-known Belgian organizations, F.O.R.E.A.M.I., F.O.M.U.L.A.C., F.S.Ki., Congo Red Cross, missions, dispensaries and private practitioners, (4) medical teaching facilities provided by Government, missions and other organizations, (5) hospitals, dispensaries and laboratories, (6) port and urban hygiene, industrial hygiene and general sanitation and (7) statistical appendices.

The following points are noted as of special interest in 1947. There were 34 cases of *plague* (6 bubonic, 24 pneumonic and 4 septicaemic), with 29 deaths, in the Lake Albert focus and 7 cases (3 bubonic and 4 pneumonic) with 6 deaths in Lake Edward focus. Vigorous measures against rats were in operation and 197,896 persons received anti-plague vaccination. There were no cases of *yellow fever* or *cholera*. In addition to 2,281 cases of *smallpox* with 11 deaths among Africans, there were 4 cases of variola minor in Europeans (1 in Léopoldville Province and 3 in Equator Province). Over half a million vaccinations and nearly a million revaccinations were done during the year.

There were 137 African and 49 European cases of *exanthematic typhus*, with no deaths recorded ; 113 of the former and 27 of the latter occurred in Léopoldville Province, where the disease appears to prevail. In Katanga, 4 European and 11 African cases of *murine typhus* were reported.

There were 3 European cases of *cerebrospinal meningitis* (1 each in the provinces of Léopoldville, Kasai and Katanga) and 248 cases with 121 deaths in Africans. Vaccination against the disease was done on a large scale.

Twenty-six cases of *trachoma* were seen in Africans in Katanga, where alone the disease seems to be endemic.

There were 4,035 European cases of *malaria*, with 14 deaths (0·34 per cent.), one-third of them occurring in Katanga Province. Thirty-two cases of *blackwater fever* with 9 deaths are reported in Europeans and 27 with 3 deaths in Africans ; again Katanga was the area principally concerned. Ten cases of *sleeping sickness* occurred in Europeans, with no deaths ; 9,289 new cases were recorded in Africans.

It is noted that 3 Europeans suffered from *yaws*, and one acquired *leprosy*.

There were 467 Europeans affected with *amoebic dysentery*, with one death, and 13,012 Africans with 128 deaths. The satisfactory decrease in mortality (0·98 per cent. compared with 1·59 per cent. in 1946 and 3·51 per cent. in 1942)

is attributed to increased use of effective therapy. The problem is being attacked vigorously *au pair* with helminthic infections and it is pointed out that, in urban and rural areas alike, the campaign against insect-borne disease should take account of these conditions.

There were 33 cases of rectal and 32 of vesical *schistosomiasis* in Europeans ; the figures for Africans were 7,539 and 1,174. *Filariasis* [no further details given] occurred in 435 Europeans and 6,397 Africans.

Six cases of *rabies* were reported in Africans (2 each in the provinces of Kasai, Katanga and the Eastern Province). There was one case in a European in Kasai [it is stated that this case was "*suivi de guérison*" and that of the 6 African cases only 5 died ; this, as worded, would imply two recoveries from rabies ; it is presumed that these cases were of *suspected* rabies].

The chapters in the Report which deal with the various medical services are full and informative. It is noted that 67,748 laboratory examinations were made and that 45,408 of these were Wassermann tests.

General hygienic measures such as antimosquito measures and destruction of rats are dealt with statistically, as are the services provided for workers in various industrial occupations and the conditions from which they suffer.

This report constitutes an excellent account of the medical services in the Belgian Congo during the year. *H. J. O'D. Burke-Gaffney*

AFRIQUE OCCIDENTALE FRANÇAISE. Rapport sur le fonctionnement technique de l'Institut Pasteur de l'Afrique Occidentale Française en 1946 [DURIEUX, C.]. [**Technical Report of the Pasteur Institute in French West Africa in 1946.**] 102 pp. 1948. Dakar : Grande Imprimerie Africaine.

The activity of the different laboratories concerned in this Report followed on the lines of the previous year [this *Bulletin*, 1947, v. 44, 1023]. The total number of specimens examined amounted to 33,617, consisting of 17,714 bacteriological, cytological and parasitological, 13,091 serological, 443 pathological and 2,369 chemical investigations. About half of these were derived from medical organizations in Dakar and the remainder from the Services and other sources.

Altogether, over 5 million doses (or cc.) of various biological products were prepared. There were over 4 million doses of yellow fever vaccine produced and over 2½ million people received the vaccine during the year, bringing the total now vaccinated by the Pasteur Institute at Dakar up to over 17 million.

The author notes once more the difficulty of keeping white mice for protection tests, and measures are being investigated to improve the housing and feeding of these animals. Nevertheless 237 protection tests for yellow fever were carried out (207 human, 30 animal). Most of the sera came from the native inhabitants of two villages where vaccination against yellow fever had been done systematically four and seven years earlier ; 24 specimens were from Europeans who had been vaccinated in various countries. Detailed tables show, in the case of the two villages referred to above, that between the fourth and seventh year after vaccination the number of strongly positive protective tests fell from 79 per cent. to 51 per cent., while the weakly positives rose from 6·6 to 30·6 per cent. during the same period ; the negatives only increased by 4 per cent. The author believes that yellow fever vaccination should be repeated within four to five years if an adequately immune population is to be maintained, and statistical tables in the text support this view.

Positive protection tests were found in 5 of 30 monkeys (Cynocephalus) examined ; all came from Kindia, in Guinea. Two human sera were examined diagnostically. One, in a child, gave a strong positive result, but the child had been vaccinated against yellow fever. The other, in a European

adult who had been vaccinated 7 months before, gave a weak positive result ; the patient died and histological lesions of yellow fever were found in tissue specimens. This anomalous case is discussed at length.

A whole chapter is devoted to the subject of rabies vaccine and vaccination. During the year 19,648 ampoules of 6 cc. of antirabic vaccine for human treatment and 965 ampoules of 20 cc. for veterinary use were prepared. Forty-six treatments were given at the Institute in 1946. The cases treated there and in other centres in 1945 are shown in statistical detail. There were no paralytic accidents and only one death, and this may have been from intercurrent infection.

The remainder of the Report gives detailed statistical accounts and observations on the general laboratory examinations and the diseases encountered. There are a number of short papers on researches undertaken, some of which have already been noted in this *Bulletin*.

The Report is well presented and gives a very informative account of the work of the Institute and its related services. *H. J. O'D. Burke-Gaffney*

PRIDI [? PRIDIE]. **Report on the Health Services of Iraq with special reference to the Incidence and Control of Endemic Diseases.** *J. Roy. Faculty of Med. of Iraq.* 1948, July–Oct., v. 12, Nos. 4/5, 135–42.

This report summarizes in general terms the epidemiological features of the communicable diseases which are of major public health importance in Iraq ; it is devoid of statistics. The chief endemic diseases are malaria, tuberculosis, schistosomiasis, hookworm disease, relapsing fever, typhus, trachoma and dysentery.

Malaria.—The newly-formed Malaria Institute had the benefit of the basic malaria surveys carried out by the British Army malaria units during the war years. Rural malaria in Kurdistan is conveyed by *Anopheles superpictus* and control measures include residual spraying and anti-larval work. In the areas of the Middle Euphrates drainage and canalization are important. In urban malaria, the " usual methods " are employed.

Tuberculosis.—A tuberculosis expert is to be appointed to survey the position and advise the Government ; meanwhile a tuberculosis hospital is being built north of Baghdad and will be used as a diagnostic as well as treatment centre.

Schistosomiasis.—A very severe recurrent infection of man with *S. haematobium* occurs in the Lower Euphrates area ; increase in irrigation will make matters worse. Elsewhere in Iraq, distribution of schistosomiasis is patchy but the situation has merited the appointment of a specialist in schistosomiasis to survey the position and advise the Government ; the provision of an anti-schistosomiasis institute is suggested where field measures and mass treatments would be organized.

Improvements in water supplies and sanitation are necessary for the reduction of the incidence of hookworm, typhoid and dysentery. Relapsing fever and typhus are prevalent and until the standard of living and personal cleanliness can be raised, anti-louse measures are applied. Trachoma and other infective eye diseases are best dealt with by fly destruction by residual insecticides and the early diagnosis and prompt treatment of cases.

The health and medical services have developed over 25 years to form a " well organised efficient machine " with adequate facilities for training health and medical staff and quite capable of dealing with existing endemic disease. The author recommends that a whole-time professor of public health be appointed at the medical school in Baghdad, and that a principal Matron is necessary for the supervision of the nursing staffs and for inspection particularly

of provincial hospitals; he stresses the importance of the closest personal contact between the Medical Headquarters in Baghdad and the members of the medical services in the country, to ensure, as far as possible, a loyal, well-trained, contented and efficient staff. *R. Ford Tredre*

SHAUL, J. R. H. & MYBURGH, C. A. L. **A Sample Survey of the African Population of Southern Rhodesia.** *Population Studies.* 1948, Dec., v. 2, No. 3, 339–53.

CLERC, M. L'évolution dans la protection sanitaire du pèlerinage de la Mecque. [**Evolution of Sanitary Control of the Mecca Pilgrimage.**] *Ann. d'Hyg. Pub., Indust. et Sociale.* 1948, Nov.–Dec., v. 26, No. 6, 194–9.

Brief reference is made to the important rôle which the Mecca Pilgrimage once played in the dissemination of cholera and other pestilential diseases about the world and the measures imposed by successive International Sanitary Conventions to cope with the evil. The Convention was last revised in 1926. Noteworthy results were achieved. Mecca has been free from cholera for thirty years or so. In recent years the health authorities of the Government of the Hedjaz have made an important contribution to the protection of the health of pilgrims and to the improvement of the sanitary conditions of its own population.

The development of air communications has introduced new dangers. Yellow fever has now to be considered as a potential danger: that disease is now known to be endemic in territories that extend right across the African continent.

The Epidemiology and Quarantine Committee of the World Health Organization has drafted new regulations for consideration at the next International Sanitary Conference. These proposals include the compulsory vaccination of prospective pilgrims against yellow fever, as well as against cholera and smallpox, if they come from countries in which yellow fever is endemic. Further studies are recommended concerning the choice of cholera antigens producing a high degree of immunity. Vaccination against typhus fever should not be insisted on, but pilgrims who come from countries in which that disease prevails should be "deloused." The Government of Saudi Arabia would undertake to keep all interested Governments informed of epidemiological occurrences during the pilgrimage and during two months before and two months after that event. If the pilgrimage has passed without any outbreak of cholera, plague, yellow fever, smallpox or typhus, north-bound returning pilgrim ships would no longer be required to go to the El Tor quarantine station; they would be merely inspected at Suez. *Norman White*

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